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Digital Image Sensor Integration in the Scope of EyeFundusScope: a Retinal Imaging System for Mobile Diabetic Retinopathy Assessment

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"It's the time you have wasted for your rose, that makes your rose so important"
Antoine de Saint-Exupéry, The Little Prince

Abstract

Diabetic Retinopathy is a pathology, asymptomatic in early stages, that is a consequence of diabetes mellitus, a disease that affects millions of people worldwide. Specifically on people with Diabetic Retinopathy, long periods of hyperglycemia lead to the creation of very fragile blood vessels in the retina, or to the suppression of old ones, leading to problems like hemorrhages or exudates, that may cause blindness.

Diabetic Retinopathy can be diagnosed with several devices, but these are mainly too expensive and non-portable, not allowing the screening of a great part of the population. This way, EyeFundusScope was created, being a smartphone based, non-mydriatic, handheld and low-cost Embedded Retinal Imaging System. Image quality depends on the system's optical alignment and it should provide fundus images with a wide field-of-view.

A communication protocol for streaming video and capturing still fundus images, from an UVC-Compliant Camera was developed, after a careful examination of the types of cameras that could be integrated in the system. Such cameras can be placed meticulously in the compact optical system, and suppress issues related to the different specifications of smartphone cameras, that often vary according to the manufacturers. An approach for low level control of high resolution and low cost camera modules was also evaluated.

With the system developed, the user can select Internal Fixation Point Actuators, that are extremely important for this diagnosis, since they allow a fixed target for the patient to fixate on, reducing image aberrations due to its eye movement and providing wider field-of-view images.

In the future, the UVC-Compliant Camera and Internal Fixation Points Actuators should be integrated on the current prototype, providing an accurate Diabetic Retinopathy screening tool which can enhance the early treatment of the pathology to a greater percentage of the population.

Keywords: Diabetic Retinopathy; Fundus Camera; UVC Compliant Cameras, Fixation Targets; Mechanical Prototyping

Resumo

A Retinopatia Diabética é uma patologia, inicialmente assintomática, consequência da diabetes *mellitus*, que afeta milhões de pessoas em todo o mundo. Assim, longos períodos de hiperglicemia levam à criação de estruturas frágeis na retina, originando problemas como hemorragias ou exudatos, que podem levar à cegueira.

Os métodos de diagnóstico da Retinopatia Diabética existentes tendem a ser muito dispendiosos e de não-portáteis, pelo que não abrangem toda a população. Assim, criou-se o EyeFundusScope, um Retinógrafo de baixo custo constituído por um protótipo mecânico acoplado ao *smartphone*, cujo objetivo é colmatar estas desvantagens.

A qualidade das imagens obtidas depende, em grande parte, do alinhamento ótico de todas as componentes do sistema, sendo que este deve conseguir providenciar imagens com um campo de visão extenso da retina.

Neste âmbito, foi efetuado um estudo cuidado dessas mesmas câmaras, para que fosse criado um protocolo de comunicação para exibir vídeo aquando da aquisição de imagens do fundo, através de uma câmara UVC. Este protocolo tem um papel importante no alinhamento ótico do protótipo, uma vez que estas câmaras podem ser colocadas no mesmo. Para além disso, estas podem suprimir problemas relacionados com as diferentes especificações dos *smartphones*, que variam consoante o fabricante. O possível controlo de alguns dos parâmetros destas câmaras também foi avaliado.

O protocolo criado permite ainda a interação do utilizador com Pontos de Fixação Internos, que criam um ponto fixo que evita artefactos provenientes do movimento ocular e aumenta o campo de visão para diagnóstico.

No futuro a câmara UVC e os Pontos de Fixação deverão ser integrados no protótipo atual, para criar uma ferramenta de diagnóstico da Retinopatia Diabética precisa, que permitirá o tratamento atempado da mesma a uma maior percentagem de população.

Palavras-Chave: Retinopatia Diabética; Retinógrafo; Câmaras UVC; Pontos de Fixação; Prototipagem mecânica

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Acronyms

ADC	Analog to Digital Converter.
AFOV	Angular Field of View.
API	App Programming Interface.
BW	Band Width.
CCD	Charged-Coupled Device.
CMOS	Metal Oxide Semi-Conductor.
CT	Camera Terminal.
DICOM	Digital Imaging and Communications in Medicine.
DR	Diabetic Retinopathy.
EFS	EyeFundusScope.
FA	Fluorescence Angiography.
FOV	Field of View.
FP	Fundus Photography.
HDR	High Dynamic Range.
IR	Infra Red.
ISP	Image Signal Processors.
IT	Input Terminal.
JNI	Java Native Interface.
MJPEG	Motion JPEG.

NDK	Native Development Kit.
NIR	Near Infra Red.
NoIR	No Infra Red Filter.
OS	Operative System.
OT	Output Terminal.
OTG	On-The-Go.
PACS	Picture Archiving and Communication System.
PNG	Portable Network Graphic.
PU	Processing Unit.
RGB	Red-Green-Blue Color Model.
SS	SuperSpeed USB.
TS	Transport Stream.
UI	User Inteface.
USB	Universal Serial Bus.
UVC	USB Video Class.

Chapter 1

Introduction

1.1 Contextualization

Diabetes *mellitus* is a disease that affects millions of people around the world, and that may lead to complications such as Diabetic Retinopathy (DR), a pathology that affects the retina in a cumulative way. Due to its asymptomatic nature, it is one of the main causes of avoidable blindness at adult age [1].

In 2010, DR affected around 127 million people, and it is predicted that in 2030 this number will grow to 191 million people. It is also estimated that the number of patients with a great probability of blindness will increase from 37 million (in 2010) to 56 million in 2030, if prevention measures, such as a correct and early on diagnosis, are not implemented meanwhile. The estimated values are based on factors such as the increasing of elderly population and obesity cases resulting from incorrect eating and a sedentary lifestyle [1].

The purpose of an effective screening program for diabetic retinopathy is to determine who needs to be referred to an ophthalmologist for close follow-up, treatment and who may simply be screened annually [2].

Currently there already exist a few diagnosis mediums for DR assessment, being the most common:

- Ophthalmoscopes
- Table-top Fundus Cameras
- Handheld Fundus Cameras

Even though the most commonly used diagnosis method is through Table-Top, non-mydriatic Fundus Cameras, these are very expensive and non-portable. This raises a big problem in terms of making the diagnosis available for affordable to everyone, especially in rural areas.

To aggravate the problem, there is also a great lack of ophthalmologists and diagnosis/treatment resources in these areas [1].

Thus, there is a great necessity for the creation of less expensive and portable medical diagnosis devices, so that a larger number of the population has access to this solutions. Despite the existence of such devices, in 2016 the British Diabetic Association, that supports the largest DR screening in the world and that evaluates new retinal cameras every six months, stated that "As of May 2016 no handheld retinal cameras appear on their approval list of 20 non-mydriatic retinal cameras for retinal screening".

It's in this context that the work here presented gets relevance, with the goal of suppressing some obstacles, such as optical alignment and camera characteristics issues, in the scope of EyeFundusScope (EFS), a project developed by Fraunhofer Portugal Research, for DR assessment.

1.2 Motivation

EFS is a Portable Imaging System, and its prototype consists in a handheld device, with a smartphone support case. The handheld device includes an appropriated optical system, integrating several lenses, and EFS Light Control, to allow the controlled illumination of the Ocular Fundus, constituted by the fovea, optical disc, retina and macula.

The fundus image is captured by the smartphone camera. The image processing is based on machine learning algorithms, that detect certain characteristics of the pathology, like exudates or hemorrhages, due to the burst of capillaries and blood vessels [3].

Given the common obstacles presented by this type of acquisition, such as the smartphone cameras being in constant evolution by manufacturers and the need for a perfectly aligned optical system, an approach for low level control of high resolution and low cost camera modules should be investigated, as a substitute for the smartphone cameras.

Besides, for an accurate diagnosis, it's required that the patient under examination keeps it's eye focused on a given point, to suppress eye movements that may blur the final image. This points are also a good feature to capture different areas of the fundus, and therefore provide a final image with wider Field of View (FOV). Thus Internal Fixation Targets should also be integrated within the current EFS prototype.

1.3 Objectives

Given the aspects referred in the Motivation (Section 1.2), the main objectives of this thesis are:

- Research the use of dedicated camera boards, to use in the prototype developed by Fraunhofer.

- Evaluate the use of UVC compliant cameras, because they are natively supported by most operative systems.
- Establish a communication protocol to allow the Android smartphone to control the camera and to display a preview stream during capture.
- Investigate the possible control of a fundus illumination system simultaneously to the image acquisition system, with the same Android application.
- Develop an approach for low level (highly parametrized) control of high resolution and low cost camera modules.
- Define a protocol for data acquisition with actuators for internal fixation points.

Given the complexity and the range of camera solutions available in the market, the use of dedicated camera boards and UVC-Compliant cameras must be evaluated, thus selecting a camera that could be integrated in Fraunhofer EFS prototype.

In order to capture fundus images, the fundus of the retina needs to be perfectly aligned with the device. Thus, the examiner has to hold the device with one hand, and move it closest or further away from the patient's eye, in order to center the ocular disc and have a clear image of the macula and fovea. For this to be possible, it is required that a real-time preview of the fundus is available on the smartphone's screen while the application is in use. This means that the capture of the image, as well as the adjustable parameters must be done simultaneously to image capturing. As such, the fourth objective of this thesis is, as mentioned, to establish a communication protocol between Android devices and cameras modules, for the control and display of a video stream during capture.

The low level control of the high resolution camera modules is an important feature, and this thesis should point out the possibility of such control, since the fundus images obtained are taken in low-light environment conditions that many times require image parameters to be adjusted.

Finally, user control of internal fixation point actuators should be added to the Android application, to provide a wider FOV of the final image and to provide a fixation target to minimize eye movements that may blur the final images.

1.4 Overview

This master thesis is divided in six main Chapters, organized for an easier understanding of the themes studied in this thesis. In Chapter 1 the reasons that support the thesis were presented, as well as the contextualization of the problem, that approaches the high relevance of EyeFundusScope (EFS) for people with Diabetes Mellitus, and more specifically, patients with Diabetic Retinopathy (DR). The Objectives were also defined to set a starting point for this work.

The Chapter 2, referring the Theoretical Concepts, addresses the theory that supports the Proposed Approach, including important concepts for handling and better understanding cameras' functioning.

The available devices for DR assessment, including Table-Top and Handheld fundus cameras are discussed in the Literature Review that constitutes Chapter 3.

Chapter 4 outlines the Approach followed, describing the development of CameraApp, the Android application created in this work, for full control of UVC-Compliant cameras, selected for integration in the EFS prototype after a thorough research, and Internal Fixation Point Actuators.

In Chapter 5, the results obtained with the approach followed by this thesis will be presented, and in Chapter 6 discussed and analyzed, in order to find what could be concluded from the present work and what could be done to improve it in the future.

Chapter 2

Theoretical Concepts

2.1 Optics of the Human Eye

Since DR is a pathology that affects vision, some aspects about the eye's anatomy must be taken in account, namely the structures that constitute this organ. The human visual system, as well as other vertebrates is constituted by three major components that work together, the eyes, that capture light and turn it into stimulus that are transmitted to the brain and processed by it, the visual path, that modifies and transmits those stimulus since they are received by the eye until they reach the brain, and finally, the visual centers of the brain, that interpret the information received so that they can form a reaction to it [4].

Vision works based on the reflection and absorption of light, when it interacts with the surface of an object, providing information about the presence/absence of those, as well as its structure and composition [4].

When light propagates in Air, it has a velocity of 3.0E8 m/s, that represents a refractive index of n=1, as stated by SI Unit Measurement system. This value depends on the medium the light it is propagating in. When entering the eye through the Cornea, a layer with only 0.5mm thickness, its refractive index is n=1.377. Then it reaches the anterior chamber, with a lower refractive index, of n=1.336, and a thickness of 3.04mm, ending at the Iris. This path, causes the light rays to get closer together, as it is seen in Figure 2.1 [5].

The Iris regulates the amount of light that enters the eye, since it's a diaphragm of variable diameter, which controls the numerical aperture and the radiance entering the eye [5].

By then, a lens of variable shape and size changes its refractive power, so that the eye can accommodate to an object a certain distance. Behind the lens, the light passes through the vitreous humor and it's received at the retina where the detection of light takes place.

The Fovea, central area of the retina, is an important structure for DR detection, since it's the region where the light is most focused on when the eye is focused on a certain object, therefore it is the portion of the retina that presents the best image detail. This structure is a small gap inside the Macula, that by its end is a 4mm diameter yellow point, next to the center of the posterior retina [6].

It's through the Optical Disc that the central artery of the retina enters the eye, and the central vein of the retina and the optical nerve exit, providing the connection to the brain. The ramifications of this vessels spread around the surface of the retina. The optical disc does not contain photo-receptor cells, reason why it is known as the blind spot of the eye [6].

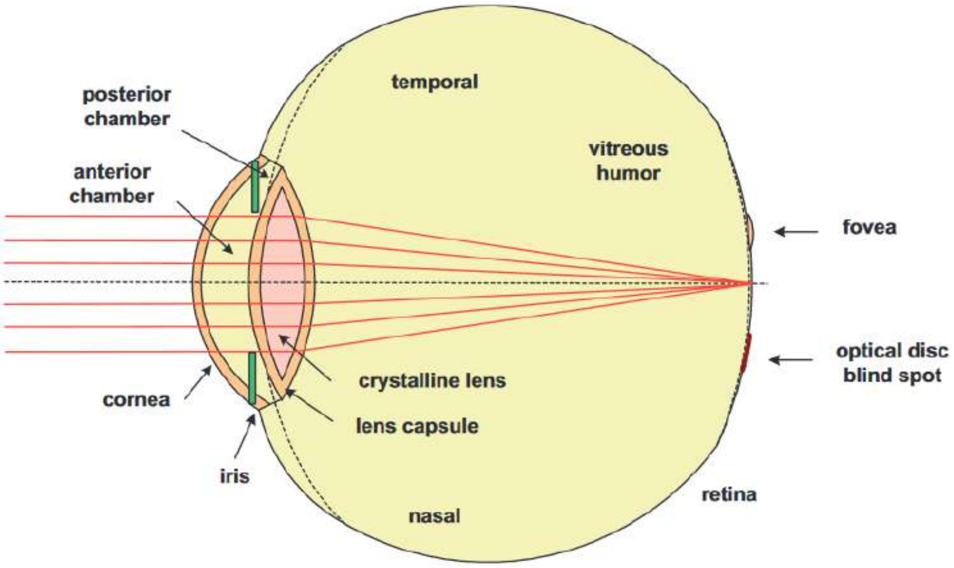


Figure 2.1: Fundus photograph of the right eye. It is possible to see the most relevant structures of the retina. Adapted from [5].

The eye has three chambers (Figure 2.1), an anterior small chamber, mentioned before, a posterior chamber and a vitreous chamber. The anterior chamber is located between the cornea and the iris, and the posterior between the iris and the lens. Both of these contain aqueous humor inside, to help maintain the intraocular pressure, which helps maintain the approximately spherical form of the ocular globe [6].

It is normal to use an analogy between the filming camera and the human eye, since both of them are optical structures, with the goal of capturing visual images resulting from the interaction of light (namely through absorption, transmission and reflection) with different materials. Both have a lens system and a variable aperture, which in the eye is the pupil. In the cameras there is the film, where the image is formed, which in the eye corresponds to the retina [6].

2.2 Diabetic Retinopathy

Diabetes mellitus is a metabolic disease characterized by hyperglycemia, which results from a flaw in the production of insulin and/or its non-actuation, even if it is produced. If this flaw is not controlled, hyperglycemia may lead to the bad functioning of several organs, specially the eyes, kidneys, nerves and blood vessels. In extreme cases it can lead to the total failure of one or more of this organs [7].

Individuals diagnosed with Diabetes mellitus may develop a complication derived from this disease, that is known as Diabetic Retinopathy (DR). This pathology begins for being asymptomatic, that causing it to be the main cause of avoidable blindness in the World [7].

Given the case where a person with diabetes mellitus goes through a long period of hyperglycemia, it's possible there is an accumulation of fluid inside the ocular lens, that controls the focus of the viewed images.

This liquid accumulation leads to changes in the curvature of the lens, and therefore the vision gets blurred. This symptoms may improve as soon as the glycemia levels are normalized.

There are two known types of DR, that differ in the way the blood vessels are affected by diabetes mellitus: [7]

- **Proliferative DR** - It's a result of the abnormal growth of new blood vessels in the retina, the optical disc or inside the vitreous cavity. Due to the fragile nature of this new vessels, there is a great probability for them to collapse, originating hemorrhages and/or detaching from the retina, possibly leading to blindness [8].

- **Non-proliferative DR** - The deterioration of the blood vessels in the retina is the cause of this type of DR, causing blood shed that can generate microaneurysms, intra-retina hemorrhages and ocular edemas (liquid accumulation inside the eye). Besides blood vessels, there are capillaries in the eye that contain lipids. These can also burst, leading to hard and soft exudates. Non-Proliferative DR can be classified according to its severity, thus if there is at least one microaneurysm, it's classified as mild state. The presence of blood hemorrhages leads to the moderate state and the severe state happens when there is more than 20 hemorrhages in 4 quadrants, vessel distention in 2 quadrants or intraretinal microvascular abnormalities in 1 of the quadrants [7–9]

There are several imaging methods to diagnose DR. For the purpose of this thesis only the non-invasive ones will be approached, since EFS purpose is insert in this category.

2.3 Fundus Photography

Fundus Photography (FP) is based on the principle of indirect ophthalmoscopy, where a digital camera is set at a certain distance from the eye, that usually varies between 5 to 50 mm. The camera's lens has the capacity to, simultaneously, transmit rays of light into the eye and collect the reflected rays, providing an amplified image of the fundus, as illustrated in the top row of Figure 2.2.

Some FP devices can be non-mydriatic, which means there is no need to dilate the eye through pharmacological agents. This constitutes a big advantage, since that forced dilation is extremely incommode for the patient undergoing the diagnosis [10].

As described in Section 2.2, in Figure 2.2 B and C, it is possible to observe the fundus of a subject with DR. In this particular case some significant structures, characteristic of DR can be seen, such as exudates, due to capillaries rupture that caused lipids leakage, hemorrhages, caused by blood vessels burst, and microaneurysms, with the appearance of small and well-defined red dots. For this last case it's important to mention that microaneurysms' size grows according to the stage of the pathology. In early stages these are about 25-125 μm. Given this fact, fundus cameras should have a high resolution, that is needed for an early diagnosis of the pathology. [9].

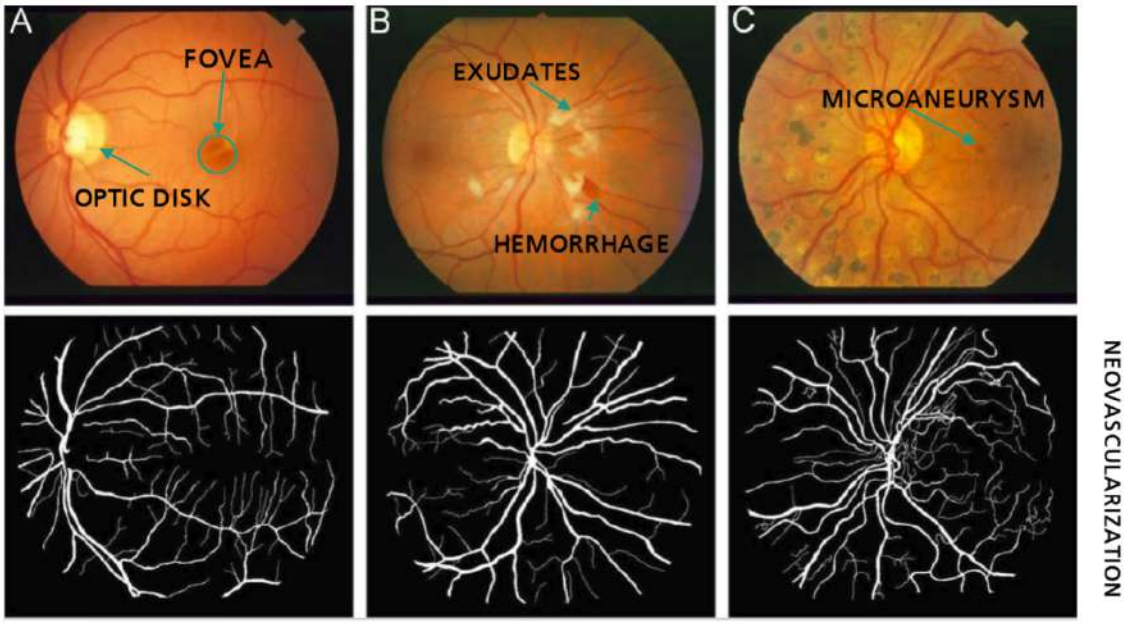


Figure 2.2: Fundus Photographs obtained from fundus cameras. A represents a healthy fundus. Figures B and C represent DR affected fundus, given the existence of exudates, hemorrhages and microaneurysms, resultant from the neovascularization described on the images bellow. Adapted from [11].

In order to understand how FP cameras work, a few of its characteristics must be known, being the most important concepts: [12]

- **Angular Field of View (AFOV)** - Full angle, in degrees, associated with the horizontal dimension (width) of the sensor that the lens is to be used with;
- **Focal Length, *f*** - Defines the lens' AFOV. It is the calculation of an optical distance from the point where light rays converge to form a sharp image of an object to

the digital image sensor. For a given sensor size, the shorter the focal length, the wider the AFOV of the lens. This way, the AFOV can be calculated according to the equation 2.1, on which h represents the horizontal dimension of the sensor and f the focal length, all measured in millimeters.

$$AFOV(^{o}) = 2xtan^{-1}\frac{h}{2f} \tag{2.1}$$

- **Spatial Resolution -** Defined as the minimum distance between two image pixels, formed by the intersection of a column and a row that form the digital image, in order to distinguish them. Thus the image resolution is given by the number of pixels that form the image obtained [13].

- **Image Sensor -** Cameras are constituted by image sensors, that process the image, considered aspects such as pixel size and distribution, or light sensitivity, as described in section 2.4.

- **Optics System Quality -** Optical Systems for DR assessment include a number of optics materials, such as optical lenses and mirrors, through which rays of light pass. Some of this rays will reach the retina, while others undergo the inverse process, thus providing an image of the human fundus. If the components that constitute this systems are not in perfect condition, or the design isn't perfectly aligned, optical aberrations will surge, possibly leading to diagnosis errors [3].

Besides the characteristics mentioned, it's relevant to understand the difference between the AFOV of a camera and the FOV of an image, since it is an important feature of the obtained image of the fundus. The FOV is influenced by the optical composition of the lens, and it indicates the area of the image (in this case, the retina) that the lens will cover at a certain distance, which means that it indicates the angle through which a device can capture electromagnetic radiation. Because of this aspect, the FOV of a camera it's usually measured in angles [14].

A FOV of 30º is usually considered the normal angle of visualization, generating a plane fundus image 2.5 times bigger then the real image. There are cameras with FOV's between 45º and 60º, however, one must remember that cameras with bigger FOV's usually require pupil's with wider diameters [14].

In order for Fundus Photography or Recording Systems to be approved, thus be commercialized as a diagnosis support system for DR assessment, the requisites established by the *International Standard for Ophthalmic Instruments - Fundus cameras (ISO 10940:2009)* must be fulfilled, since this protocol specifies the necessary requirements and test methods.

The following listed tests are part of the full test list that must be performed for the approval of the optical system as a DR assessment diagnosis, as stated in *ISO 10940:2009*. The tests mentioned are the only ones applicable to the camera selection, therefore these are the only ones refereed to in this thesis. For the complete approval of the system there are a few more tests, namely related to the optical path, that need to be fulfilled [15].

- **Check the Resolving power of the fundus camera optics -** The test targets images from the center, middle and periphery used for checking resolving power.
- **Check the Field-of-View -** The check shall be done by taking a picture of a graduated target (i.e. millimeter paper), placed 1 m from the entrance pupil of the fundus camera. The scale has to be perpendicular to the optical axis and centered to the field of view. From the image obtained, the distance 2r can then me measured, in millimeters, from edge to edge on the image of the visible scale. The angular field of view is then found according to the equation:

$$FOV(^{o}) = 2(arctan(\frac{r}{1000})) \tag{2.2}$$

It should also be referred that there are other techniques that also use a camera coupled to an image processor, as is the case of Fluorescence Angiography (FA). Due to this reason, FA was used during many years to diagnose pathologies related to the retina, as instance DR. However, it is being surpassed by the FP technique, because FA has the disadvantage of having to rely on an intravenous injection of fluorescent sodium to obtain the fundus image [14].

2.4 Camera Concepts

In order to select a camera to integrate in the EFS prototype, it's necessary to have a wide background knowledge about the components that constitute this devices, since its components affect the fundus image that constitutes the final outcome of this process.

One of the most important parts of the camera's optical system is the sensor, that contains millions of pixels for image resolution, and creates the conversion of an analog image into a digital one [16].

It's the combination between the camera's sensor, lens and image processor that dictates the quality of the image produced, therefore even if two cameras have the exact same sensor, the image obtained can be very different from each other [16].

The simplified block diagram in Figure 2.4 represents the architecture behind camera's functioning. First, the scene is focused on the image sensor, using imaging optics, the group constituted by an optical lens and the image sensor. The focal length of a lens depends, not only on the lens itself, but also on the sensor used, and more specifically on its size.

As represented by the scheme on Figure 2.3, for smaller sensor sizes, using the same lens for imaging, the image will appear more cropped, thus the AFOV of a camera with this sensor, will be smaller. This factor can be measured by the crop factor, that is standardized as n=1 for full frame sensors, that provide a film pane of exactly 36 x 24 mm [17].

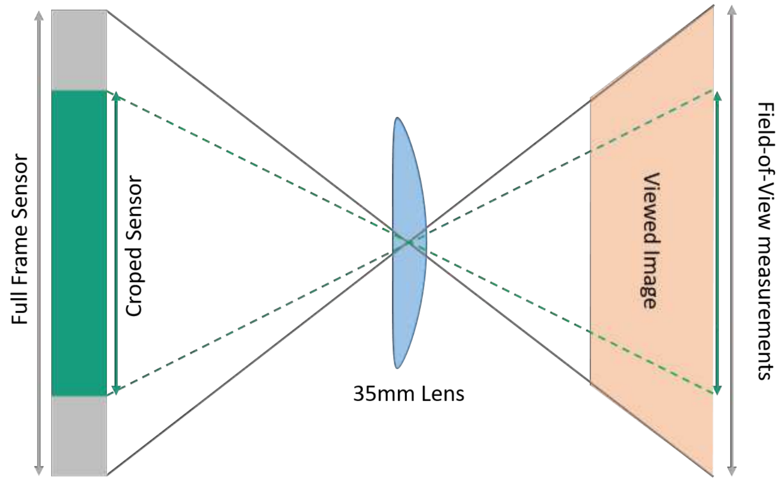


Figure 2.3: Schematics of the AFOV representation for two cameras using the same lens and sensors with different sizes.

The incident light is then converted into an array of electrical signals by a two-dimensional array of pixels. Color imaging is done by the use of a color-filtered array. In this specific case, a Red-Green-Blue Color Model (RGB) filter is used. This filter causes each pixel to produce a signal corresponding to only one of these three colors. The analog pixel data (i.e. the electrical signals) are then read out of the image sensor and digitized by an Analog to Digital Converter (ADC) converter, producing a full color image, with green, blue and red values for each pixel in that image, as well as a spatial interpolation operation, known as *demosaicking* [18].

After this operations are performed, Image Signal Processors (ISP) functionalities can still be added, for white-balance, auto-focus, auto-exposure and color correction operations, as well as to diminish the adverse effects of fault pixels and imperfect optics. The final step of the process is the image compression and memory storing [18].

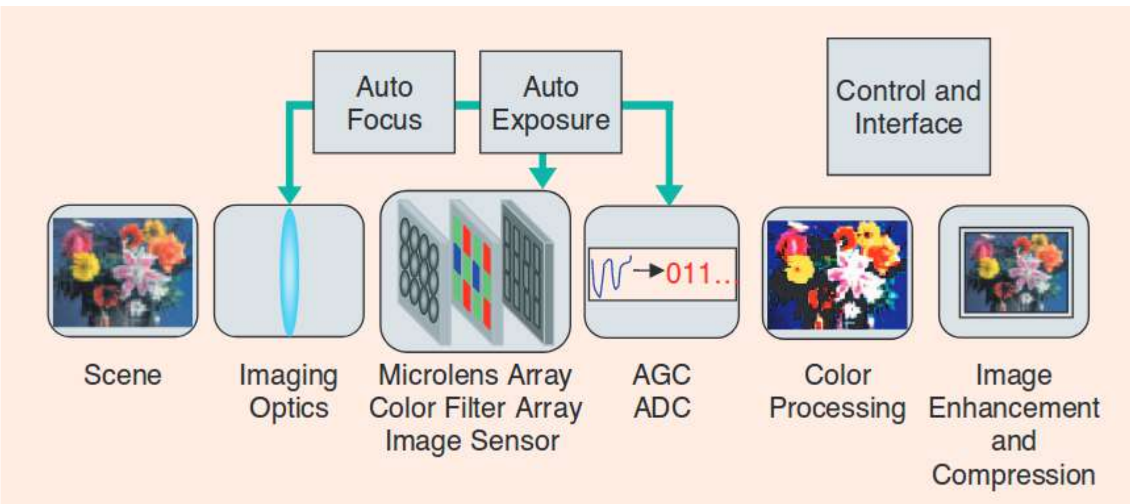


Figure 2.4: Imaging System simplified block diagram [18].

Image sensors consist on arrays of pixels, each containing a photodetector for incident light conversion into photocurrent. Some circuits need to convert that photocurrent into eletric charge to read it. The most common sensors belong to two categories, represented in Figure 2.5: [14, 18]

- Charged-Coupled Device (CCD)
- Metal Oxide Semi-Conductor (CMOS)

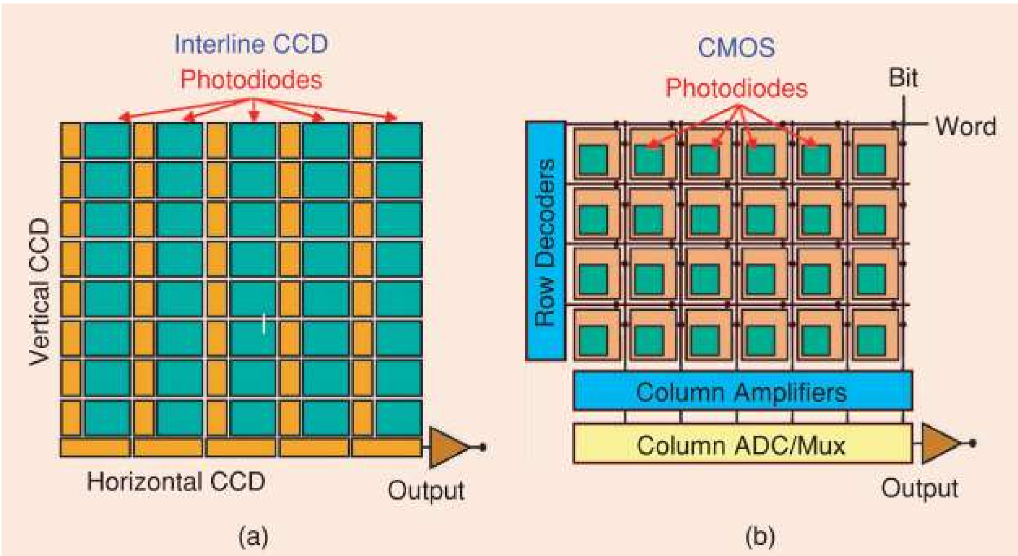


Figure 2.5: Camera sensor types: (a) CCD sensor and (b) CMOS sensor architectures [18].

Invented in 1970, CCD is a silicon sensor, constituted by a series of photosensitive circuits ((a) in Figure 2.5), that move the charges inside the sensor. This is a sequential logic circuit, therefore it needs two clocks for set or reset states, simultaneously. The CCD sensor is an analog device, however, its output is immediately converted in a digital signal through an ADC, that exists in digital cameras [14, 19].

Before reaching the exit amplifier, the charges must be transferred, and the limited velocity at which this transfer occurs must be taken into consideration, since it leads to delays in the velocity between shoots. Apart from this delay, it's this charge's transfer that causes a bigger sensitivity and pixel-to-pixel consistency, that characterizes the CCD sensors [14].

The main advantages of using a CCD sensor are the higher quality of the images obtained (especially in low light environments), given there is less noise, better depth of color (twice the dynamic range achieved by CMOS sensors), higher resolution and greater sensitivity to light [20].

CMOS sensors are digital sensors, constituted by an integrated circuit that converts the photosensitive pixel's charge into voltage on each smaller circuit that composes it. After this conversion, CMOS possesses a multiplex system by line and column that allows the several signals obtained to be converted into just one signal, that will be sent to the multiple ADC converters presents in the camera chip (Figure 2.5 - *b*) [19].

Each smaller circuit is composed by one photodiode and three transistors. The sensor has the reset or pixel activation function, as well as the amplify/convert the charge into analog signal, and select or synthesize the information of the several signals in a single one. Therefore, the velocity of the CMOS sensors is far greater then the CCD sensors, however, the sensibility is way smaller, and the noise that contaminate the image is bigger, what is due to the inconsistency on the several charge to voltage conversion circuits [19].

The CMOS advantages, when compared to CCD are: [19, 20].

- Lower costs, due to a lower flux of charges, or current in the CMOS sensor.
- Its ability to work with very high luminosity levels, what allows its use on dynamic reach cameras.
- Allowing the integration of stabilization systems, image treatment and compression.
- Fastest image processing. CMOS sensors are constituted by active pixels and an ADC converter on the same chip.
- Low power consumption, due to 100 times less flow of charge, when compared to CCD.

When looking for a camera to integrate with the EFS prototype, it was relevant to check for cameras without Infra Red (IR) filters, since these record short-wave IR frequencies, constituting a good feature for EFS, given the capturing is done under this low-light environment conditions.

Chapter 3

Literature Review

Fundus imaging may be obtained by several devices. The first device for fundus viewing was the ophthalmoscope, a small, handled device that didn't allow DR screening, given it's low FOV. The growing integration of technology in imaging techniques lead to the appearance of Non-mydriatic Cameras, that are an efficient DR screening technique, but aren't portable and are very expensive. To suppress this limitations, FP systems are now starting to be available in the market [21, 22].

3.1 Non-mydriatic Automated Cameras

Non-mydriatic cameras, as seen in Figure 3.1, do not require pupil dilation by the use of mydriatic agents, allowing the user to see the fundus on a digital screen, with the possibility to zoom in, perform vessel and/or lesion measurements and share those images with the patients and on Picture Archiving and Communication System (PACS) systems [22].

Figure 3.1: Non-mydriatic Automated Camera used for fundus examination [22].

Stereoscopic color fundus photography in 7 standard fields, and with a 30º FOV, is, as defined by Early Treatment Diabetic Retinopathy Study group, the Gold Standard for DR assessment in the world. Table-top fundus cameras are included in this group, being the most commonly used devices by Portuguese ophthalmologists for DR assessment. Despite their good results in terms of diagnosis accuracy, there are two main disadvantages for the use of such devices, namely the costs associated with purchase and their very low portability, since they are required to be placed on a fixed, plain surface in order to be used, therefore it becomes very difficult to transport such devices into rural areas, where the access to medical devices is a challenge [23].

3.2 Handheld Fundus Cameras

As described in Subsection 2.3, FP has been a very interesting area for engineers and developers to explore. Since Carl Zeiss, in 1926, created a 10º FOV, flash powder and color film equipped mydriatic fundus camera, FP has improved a lot. Some of the most relevant innovations are related to the appearance of nonmydriactic imaging, electronic illumination control, automated eye alignment, and high resolution digital image capture. The combination of this new features made FP a standard technique for developing and documenting retinal disease, such as DR [24].

Despite this improvements, fundus cameras still don't take full advantage of consumer camera's built-in function and space saving. Besides that, the prices of such cameras are still too high, specially for underdeveloped countries, that still face a great lack of diagnosis resources, and DR diagnosis is no exception [25].

In order to face this disadvantages, Kenneth Tran developed a study with the main goal of creating a FP device for the capture of human fundus images and the documentation of retinal pathologies, using only components under £1000. A front objective lens, positioned at 5 to 50 mm from the front of the eye was used. The purpose of this lens was to simultaneously relay light rays towards the eye and collect the reflected light, providing a view of the fundus. The camera used was Panasonic's Lumix G2 [26].

To allow a better comparison between this camera and the EFS cameras, the following characteristics of the Lumix G2 should be evaluated: [26]

- CMOS sensor
- Rapid Automatic Focus
- Exposure Capabilities
- Live-view imaging
- 12 MP resolution
- Built-in image stabilization

To increase the focusing ability, there was the need to attach a screw-in macro lens to the front lens of the Panasonic Lumix G2. The autofocus, as well as the image composition, are both performed on the camera's built-in LCD screen. The best way to obtain the desired focus is to move the focusing area of the camera over the optic nerve , since the contrast between the surrounding vasculature and the optic disc allows the camera's contrast-based autofocusing algorithms to lock the accurate focus. This way, a fundus image is acquired by following a point-and-shoot operation sequence [26].

Figure 3.2: Hand-held, low cost fundus camera prototype developed in [26].

The final fundus camera prototype developed (Figure 3.5) was able to be used in a handheld portable manner, with the subject sitting down in a reclined head position. The camera should be operated with both hands, while the user was standing. In most cases, the camera was used 40 to 45 mm away from the subject's eye, depending upon variances in refractive power. Both the optic nerves and macula-centered images could be obtained with the device, but only with a certain degree of subject cooperation [26].

Each image acquisition lasted 10 to 25 seconds, but this parameter, as well as image quality, depended greatly on the dilation pupil size and the reflectivity of the fundus, resulting in low, partial or vingnette exposure of the fundus. In an attempt to fix this situation, it was stated by the investigators that the user should take two to three fundus photographs to ensure satisfactory image quality for clinical diagnosis. Overall, 22 of 26 photos (85 %) taken were judged sufficient for clinical diagnosis.

Despite all this, the biggest disadvantage of the prototype created by Tran, in [26] is the need for pharmacological mydriasis, that as stated before, causes a great discomfort to subjects.

3.3 Optomed Aurora

Aurora fundus camera, developed by Optomed, is a non-mydriatic imaging system for DR detection, Figure 3.3. Its main features include: [27]

- 50º FOV.

- Compact and portable for clinics of all sizes.
- Rechargeable battery, including an Optomed dual charger for power supply.
- Image archive including Digital Imaging and Communications in Medicine (DICOM) systems.
- Minimum 3.1mm pupil size.
- 5MP camera resolution.
- 9 internal fixation targets for peripheral imaging.
- Color, red-free, IR and Low-red photography.

Figure 3.3: Optomed Aurora fundus camera [27].

3.4 OICO Fundus Camera

OICO Fundus Camera is a portable, automated, non-mydriatic camera, that can also be used on manual mode, Figure 3.4.

The most relevant features of this camera are: [28]

- 30º to 35º FOV, depending on pupil size.
- Pupil must be at least 3.5mm, without dilation.
- Build-in camera with 12MP resolution.
- 4h Battery autonomy. Buying the system also includes its own charger.
- White-light flash for fundus illumination and IR light for system adjustment.
- System protected with password.

- Bluetooth and WiFi system, to facilitate the information share with dropbox, Google, Microsoft or other sharing systems. Medical systems such as DICOM and PACS are also available.

Figure 3.4: OICO fundus camera [28].

This camera still has improvement points to consider, being the most relevant ones the need for diopetry compensation, that has to be inserted manually by the doctor and it doesn't possess internal fixation targets.

3.5 Volk Pictor Plus

Volk Pictor Plus is an ophtalmological device, non-mydriatic, portable and relatively light. This features make this device easy to use for examinations outside the hospital, reaching a greater number of patients.

The main characteristics of Volk Pictor Plus are: [29]

- Non-mydriatic.
- 5 MP Image sensor.
- 40º static FOV.
- 120º dynamic FOV.
- Two illumination modules: white-light, IR LEDs.
- Image transfer through Universal Serial Bus (USB) port or via WiFi network.
- AutoFocus and Automatic Shooting.
- Static and video image capture.

- Eight internal Fixation Targets.
- Pupil minimum size of 2.7 mm without pupil dilation.

Figure 3.5: Volk Pictor Plus fundus camera. Adapted from [29].

3.6 EyeFundusScope

The current prototype developed by Fraunhofer, consists in a mobile device that can illuminate the human fundus and capture images of it through a smartphone camera, as it is seen in Figure 3.6.

The main features of the EFS prototype are: [3]

- Handheld device.
- Low-cost.
- Non-mydriatic.
- 40º FOV.
- Image capture with Nexus 5X smartphone camera.
- 4mm Pupil Size.

As it happens with OICO Fundus Camera (Section 3.4), EFS doesn't integrate internal fixation targets. This aspect, as well as the integration of an internal, fixed camera on the prototype, are two important improvements, that are part of the objectives of the current work.

Figure 3.6: EyeFundusScope mechanical prototype schematics. Schematics developed with SolidWorks in [3].

3.7 Fundus Photography Cameras Comparison

In tables 3.1 and 3.2, it is possible to compare some relevant characteristics of Fundus Photography devices available in the market, namely the ones mentioned in Subsections 3.3, 3.4, 3.5, in order to establish a correlation to the solution presented by Fraunhofer's EFS, described in Subsection 3.6.

Table 3.1: Fundus Photography Devices. [28–33]

	D-Eye Ophtalmoscope	VOLK InView	VOLK Pictor Plus	Horus DEC 200	OICO Fundus Camera	Optomed Smartscope pro
FOV	20º (Mydriasis) 6º (No Mydriasis)	50º (Static) 80º (Dynamic)	40º(Static) 120º(Dynamic)	45º	30-35º	40º
Resolution (MP)	1	1	5	5	12	5
Pupil Dilation	Yes	Yes (5mm pupil minimum)	No (3mm pupil minimum)	No	No (3.5mm pupil minimum)	No (3.5mm pupil minimum)
Internal Fixation Targets	No	No	9	7	No	9

Table 3.2: Fundus Photography Devices. [3, 27, 34–36]

	Optomed Aurora	Zeiss VISUSCOUT 100	Eyenez V300	EpiCam C	EyeFundusScope
FOV	50º	40º (Static)	45º	33º(Vertical) 45º (Horizontal)	40º
Resolution (MP)	5	5	5	1.3 (USB 2.0) and 5 (USB 3.0)	12 (using Nexus 5X smartphone)
Pupil Dilation	No (3.1mm pupil minimum)	No (3.5mm pupil minimum)	No	No (4mm pupil minimum)	No (4mm pupil minimum)
Internal Fixation Targets	9	9	No	No	No

The analysis of Tables 3.1 and 3.2 allowed to the comparison of some aspects of available fundus cameras and the current EFS prototype.

The FOV of fundus cameras, as referred in *ISO 10940:2009* [15] refers to the the area of the fundus that can be imaged by this devices in single field fundus images and it has to be big enough to capture the optic nerve and the macula, always keeping a compromise with image resolution. EFS has a 40º FOV, this value has a good range for capturing this structures, despite other devices, like Aurora fundus camera, have bigger FOV values.

Despite this, single field fundus images are not always enough to reach an accurate diagnosis for DR, considering that a significant proportion of the fundus remains uncovered [25]. This factor can be compensated by adding Internal or External fixation points to the fundus camera, since these provide a fixed target for the patient to fixate, in different positions, that are acquired and then *stitched* in a wider fundus image, as will be discussed in Subsection 4.2.2.

As described on Table 3.2, EFS doesn't have internal fixation targets at this point, which is a great disadvantage when in comparison to the other devices mentioned. Thus, given this feature's importance for the system differentiation, it constituted one of the main improvement points that is a part of the objectives in the current work.

EFS is a non-mydriatic camera, which is a strong advantage in comparison to others that do not have this feature, like D-Eye Ophthalmoscope and VOLK InView fundus camera. This feature reduces patient discomfort related to pupil dilation via pharmacological substances, and eases the image acquisition for the specialized technician handling the device.

For the image acquisition, a light source is needed, since the fundus is not illuminated as is. This way, EFS uses a flash to capture the final fundus image. Another option, also studied in the beginning of this work, was the use of a camera without IR filters. This feature, enables this cameras to display low-light environment scenarios. Raspberry Pi NoIR Camera is included in this category, therefore being considered one of the solutions to integrate in the FOV prototype. Nonetheless, the use of a Raspberry Pi Computer Board would not be the best option in terms of prototyping, causing design issues and requiring additional programming.

Another consideration to EFS, that increases its commodity to the patient undergoing the examination, is the integrated illumination module. This module, also known as

Light Control, provides the user control over the light intensity, so that the light incising on the patient's eye is by one side, enough to illuminate the fundus for image acquisition, and at the same time isn't too intense that causes pain to that same patient.

3.8 Fraunhofer Enhanced Camera API

The EFS Android application uses Fraunhofer EnhancedCameraAPI library, which is a solution developed for providing a large range of parameters, as is the case of focus, exposure, white balance, digital zoom, preview and acquisition sizes, amongst others.

The main features of this library are:

- Easy configuration of Camera in Android
- Fault tolerant setup of parameters
  - Handle multiple possible options
  - Ensure that unsupported parameters are not chosen
- Low Level Control over all available parameters
- Access to individual preview frames

Retinal imaging requires very specific parameters. For the illumination of the retina, a warm white LED is needed, thus the white balance should be set to Incandescent.

Two different operation modes are also required, the alignment and acquisition mode. For the first one, since the LED intensity is low, the ISO value must be extremely high and the shutter time needs to be longer as well.

For the acquisition mode, the LED intensity is set to high, therefore the ISO value decreases and the shutter time is shorter (1/20s). More than fifteen Android smartphone's have been tested and are fully compliant with the EnhancedCameraAPI.

The controllable camera parameters released by Fraunhofer's EnhancedCameraAPI are a strong feature of this application, given the reasons presented for the importance of such control in the acquisition of fundus images for DR assessment.

Nonetheless, this API still doesn't provide a solution for the optical alignment issues and image quality if the EFS prototype isn't used with a specific smartphone, in this case the Nexus 5X smartphone, that was used for the calibration of the optical system. Besides, internal fixation target actuators cannot be controlled with this API. Therefore, this work aims to present a possible solution to improve this points, by trying to keep a set of controllable parameters as the ones controlled by the EnhancedCameraAPI.

Chapter 4

Proposed Approach

4.1 EyeFundusScope Camera Selection

The growing use of smartphones in the daily lives of the great majority of the population changed the way medical devices work today. Smartphone based imaging systems became a reality, that is relatively easy to use and to access. As EFS aims to reach population that cannot access a DR diagnosis so easily, or at all, it was first designed to use the smartphone, and therefore its camera, to photograph the ocular fundus.

Smartphone's compact cameras are the result of the development of CMOS camera sensors, that made the integration of high pixel camera lens in mobile phones possible, given their very reduced size. The FOV of mobile cameras is usually in the interval of 70º to 80º, which are large values for this characteristic [37]. This kind of cameras have very specific characteristics, that often change between manufacturers, which raises some concerns like the perfectly aligned optical system or the fundus image quality. Concerning this, the selection of a fundus camera for integration in the EFS prototype is extremely important.

CMOS sensors were chosen during the selection of a camera for EFS considering their characteristics, as described in Section 2.4:

- Lower costs, when compared to CCD sensors.
- Faster image processing, relevant for a video stream of the fundus image without delays.
- Low power consumption, important given the power source of the entire system will be the smartphone's battery.
- Reduced size, for enabling the future integration inside the EFS prototype, that aims to be a handheld device.

The EFS cameras studied include three relevant camera types: Embedded Camera Modules, Dedicated Camera Boards and UVC-Compliant Cameras.

These cameras have some characteristics in common, such as the available image sensor interface, that is usually of the parallel or MIPI type. Parallel interfaces use more than one wire to establish the communication between systems, which makes it possible for both spatial and temporal dimensions to be available for the data.

MIPI interface, namely MIPI's CSI-2 interface, is a low-power, high-speed and robust hardware interface that implements camera and imaging components in mobile devices [38].

Despite these similarities, the camera types mentioned are different in many aspects. Camera modules consist on cameras that can apply a certain level of post capture processing to the images captured. In order to make its use simpler to the developer, camera modules have built-in sensor interfaces, so that there is no need to alter the driver used to communicate with the board attached, since all camera sensors, even future ones, are supported by the camera driver supplied by the manufacturers.

Dedicated camera boards are the central module of embedded image capturing systems, Figure 4.1. They're composed by a processing chip, memory disc, power supply source and some may include ethernet, USB and/or HDMI ports. Raspberry Pi NoIR V2 camera board is an open design camera board, and it was initially studied for integration in the prototype. This camera seemed like a good option because of it's characteristics, namely its high flexibility and operational simplicity, at the cost of requiring a relatively cumbersome Raspberry Pi 1,2 or 3 computer board [39, 40].

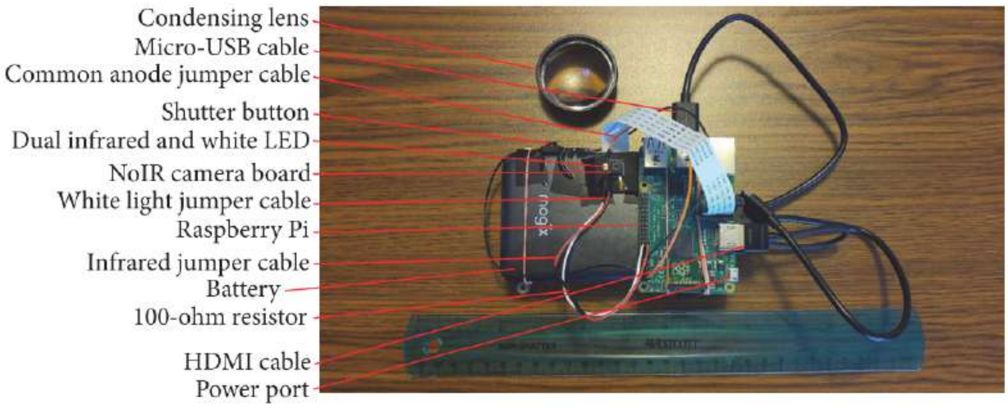


Figure 4.1: Raspberry Pi NoIR Camera Board used in [41], for the development of an inexpensive fundus camera.

Raspberry Pi NoIR V2 camera is constituted by an image sensor with 8MP image resolution, but the feature that makes this camera the most appealing for EFS integration is that it doesn't have IR filters. Without these, the camera is capable of capturing IR wavelengths, thus being a good option for the capture of low-light environment images.

With this feature, it becomes possible to capture fundus images without an illumination module. This is an important feature, since the prolonged use of a light source to illuminate the retina can damage it [40, 41].

But despite the clear advantages presented by Raspberry's NoIR Camera, there were four disadvantages that lead to the discard of this option for EFS integration. The first one is that there already was a solution for DR assessment based on this camera module, therefore the current approach wouldn't have a great differentiation from the current literature [41].

The second reason is that in terms of prototyping, it's not as advantageous to have a Raspberry Pi Computer Board in the final solution, given the space it occupies, that would require many changes to the current design.

Besides the solution would only be available for the integration of Raspberry Pi Computer Board based cameras. This would limit the solution developed, making it completely focused on a specific camera board device, thus making the solution less embracing for future cameras, with faster and better quality sensors.

The fourth reason, and the most decisive one, was that Raspberry Pi requires an external power supply. This would be a major limitation to the system's portability, since this pretends to use only the smartphone's battery as the power supply for the entire system.

Embedded camera modules are very versatile and have a wide range of options, since they can be interfaced to a specific processor, of the developers choice, or to a lens of their choice. This type of camera modules are *Plug & Play* devices, that in opposite to Dedicated Camera Boards, don't require a specific programmable Board to be connected to a device, in this case, the smartphone. For the desired solution, a *e-con Systems* embedded camera, also UVC-Compliant, Figure 4.2 was evaluated as a possibility for EFS integration, given it is a Near Infra Red (NIR) camera with a 60º AFOV value, that is within the desired range for EFS integration, and it's low price of $89. But still, given delays in the delivery of the embedded system from it's manufacturer, this option wasn't possible to integrate during the course of this thesis [42, 43].

Figure 4.2: Embedded e-CAM51_USB - 5 MP OEM USB Camera Module [43].

Finally, the last option to be considered is the use of UVC-Compliant Cameras, that are natively supported by most Operative System (OS). UVC-Compliant Cameras, commonly known as *Plug & Play* cameras, are easily plugged in Windows and Linux systems, without requiring additional device driver software. The most commonly used UVC-Compliant

Cameras have USB 2.0 or 3.0 interfaces, allowing the connection to other USB compliant devices, as is the case of the smartphone used in this thesis.

UVC-Compliant Cameras are equipped with UVC controls to adjust imaging parameters, such as brightness, contrast, hue, saturation, sharpness, black-light, gamma, white balance, exposure, gain and focus. Ascella (See3CAM_CX3ISPRDK) and Logitech C270 webcamera in Figure 4.3 were the two UVC-Compliant cameras selected for this category, as will be discussed in Subsection 4.2.1 [44].

a UVC-Compliant Camera Module - Ascella (See3CAM_CX3ISPRDK).

b Logitech C270 webcamera UVC-Compliant.

Figure 4.3: Logitech C270 and Ascella (See3CAM_CX3ISPRDK) UVC-Compliant Cameras [44, 45]

In order to select the final camera for prototype integration, an important characteristic of the camera types discussed, that had to be considered was their interface. There are two relevant USB interfaces, 2.0 and 3.0, with important variations from one another that affect, amongst other characteristics, the speed of the data transfer between devices. A more detailed analysis of this interfaces is done in Subsection 4.1.1. This is relevant for this work, since the aim is to get a connection between the UVC-Compliant Cameras and the Android smartphone, with enough speed to allow the simultaneous display and capture of the fundus image, with the lowest delay possible.

4.1.1 Universal Serial Bus (USB) Specification

USB is a personal-computer interface, established in the majority of devices, such as keyboards, computers, cameras, drives, audio and video devices, amongst others. This is a versatile technology, that primes for being very reliable, inexpensive and most importantly for being supported by most OS.

The mentioned characteristics make USB a likely solution for enabling the communication between a computer to a device, or as is the case of this work, a camera and a smartphone.

USB has had many improvements, one of which being the data transfer speed improvement, known as SuperSpeed USB (SS) and a more flexible power delivery. These features are the main distinction between USB 2.0 and 3.0 interfaces.

USB 2.0 showed that a bus 40 times faster then the previous versions, could still support both low and high speed interfaces. The ability to use several speed levels increased the complexity of the serial hubs, but managed to conserve bandwidth so that the hubs used could remain the same for both interfaces. What causes this difference in terms of data transfer speed is USB 3.0 larger Band Width (BW), causing great improvements in transfer rate, with a maximum of 400 MByte/s. This is possible due to the mass data transfer mechanism that is characteristic of the USB interface [46].

USB 3.0 interface is compatible with USB 2.0 and 3.0 hosts and hubs supporting all four speeds. This new interface was created to complement USB 2.0 specifications [46].

In conclusion, the main add-on to the USB 2.0, was the speed increase. USB 3.0 is 10 times faster then USB 2.0, plus it can carry data on both directions at the same time, thus constituting a more efficient solution [46].

In the specific case of Android smartphones, the USB interface is usually micro-USB, and it can be of several types. The most common is the micro-USB Type-B port [47].

The newest smartphone devices are equipped with USB Type-C port. This is an improvement in terms of data-transfer speed and power saving, and as it happens with the mentioned USB 3.0/3.1, micro-USB Type-C is much more simple then its previous Type-B version. USB Type-C ports have a range of 15 – 100 Watts *per* port, featuring support for the USB power delivery specification. This means that a smartphone with a USB Type-C entrance can easily charge other devices (apart from a full desktop PC). If we're referring to a micro-USB Type-B port, it ts limited to a maximum of 7.5 Watts [47].

As the purpose of this thesis includes the connection between an external camera, with an USB 2.0 or 3.0 interface and an Android smartphone with a micro- port, that will act as the host device, providing the power to support the entire system created, then an USB On-The-Go (OTG) cable must be used to fit this purpose [48].

Given this information on USB Interfaces, the best options in terms of data-transfer speed, so that the Android Application developed is as fast as possible in terms of simultaneously displaying a stream image from the camera selected for EFS, and allow image capturing is a smartphone with a micro-USB Type-C port and with a camera with USB 3.0 interface.

Despite this fact, the smartphone available for testing during this thesis was a Samsung A3 2016, with a micro-USB Type-B interface, that could only be connected to USB 2.0 compliant camera devices. Nonetheless, the application proved to be fast enough to fulfill the requirements established above, meaning that if a device with USB 3.0 interface and micro-USB Type-C is used instead of the Samsung A3 2016, the results are expected to be even better then the ones obtained.

This proves that, despite USB 3.0 interface is faster then its previous USB 2.0 version, the use of a camera with a USB 3.0 connection is not required for the good functioning of the CameraApp developed in this work.

4.2 CameraApp: Android Camera Application Development

One of the main Objectives of the present thesis is to establish a communication protocol to allow the Android smartphone to control the camera, simultaneously to the capture of fundus images by the user.

As it was mentioned in Section 4.1, UVC-Compliant Cameras are the most relevant cameras for EFS integration. This way, the USB Video Class Protocol must be studied to allow such connection.

This way, an Android Camera Application constitutes the approach developed in the thesis, allowing the communication between Android, UVC-Compliant Cameras and an ATMega2560 board, that will add an extra, and very important feature in the detection of DR, Internal Fixation Target Actuators, further discussed in this Chapter's Subsection 4.2.2.

4.2.1 USB Video Class Protocol

After a careful research of the potential camera types, in Section 4.1, and the type of USB Interfaces available, in Subsection 4.1.1, UVC-Compliant Cameras were selected as the best option to integrate in the EFS prototype. It is very important to know how to make the connection between the camera and the smartphone, in a way that the communication protocol selected in this thesis, can adapt to a wide range of UVC-Compatible devices.

Considering, UVC drivers must be evaluated, since they seem to be a good option for the solution this thesis aims to achieve.

UVC is a Microsoft-provided AVStream minidriver that provides driver support for USB Video Class Compliant Devices. This means that when a device uses UVC, there is no need to develop a new, specific driver for it, since the device will work automatically with the system-supplied driver. This protocol enables devices like webcameras, digital camcorders, analog video converters, analog and digital television tuners, amongst others, to connect seamlessly with host machines. UVC supports streaming from multiple video formats, that include Motion JPEG (MJPEG) for instance. [49].

Many OS platforms already have native support for UVC drivers, which greatly reduces the time required for developers to create USB video devices.

This way, by using UVC models, it is possible to implement video streaming hardware according to the guidelines in the USB Device class definition for video devices specification, and without having to create proprietary drivers. Besides, there is also the possibility to add vendor-specific processing to the UVC driver functionality [49].

To make sure the right smartphone-camera connection is chosen, it's important to know the main advantages of using an UVC driver:

- No need for development of proprietary drivers.
- Opportunity for vendors to add functionality.

- No maintenance cost.
- Compliant with Selective Suspend power management.

The USB Video Class protocol is provided by *USB Implementers Forum, Inc.*, and it is a specification for devices that follow Universal Serial Bus technology. This protocol describes the minimum capabilities and characteristics that a video streaming device must support to comply with the UVC specification.

Devices that follow this protocol have standardized video streaming functionality, and it provides information for designers to built UVC Compliant Devices, incorporating the video streaming functionality. A number of mandatory or optional requirements are specified, in order to help developers understand how to use the UVC protocol. [49].

The UVC protocol establishes a Video Interface class that groups all functions that can interact with USB-Compliant Video Data streams. The Video Interface is divided into subclasses, Video Control and Video Streaming Interfaces, that are used for Streaming the Video from the UVC Camera [49].

The video function is constituted by Units, that provide the basic building blocks to fully describe most video functions, and Terminals, divided in Input Terminal (IT), representing a starting point for data stream inside the video function, and Output Terminal (OT), representing an ending-point for output streams. The protocol also allows the user to make some changes to the video being displayed during the stream. For instance, Brightness, White Balance, Gamma, Contrast Controls, amongst others, can be added inside a Processing Unit (PU), by issuing appropriate requests. This way, these controls can be displayed in a User Inteface (UI) thus providing those features to be controlled [49].

Besides the mentioned terminals, that control image parameters, the UVC protocol also allows the control of some of mechanical (or equivalent digital) features of the device, known as Camera Terminal (CT) controls. These can be features like Auto-Focus, Focus and Auto-Exposure [49].

There is also the possibility for Still Image Capture, associated with the video stream, that can be done by three different methods. The one used in this thesis extracts the next available video frame from the active video pipe in the relevant Video Streaming interface upon receiving the triggered event. This way, the video stream will not be altered or interrupted, and the still image captured will have the same size as the video frames being streamed [49].

CameraApp was build using Android Studio, an Android application development environment. For the development of the application, Java Native Interface (JNI) libraries, that include the UVC-Protocol described, were imported into the code developed in this thesis, for full support for UVC-Compliant Cameras, as well as to provide some of the low-level control for this cameras [50]. This JNI libraries define the way the managed code interacts with native C/C++ code, provided by Android Native Development Kit

(NDK), that allowed the build of performance-critical parts of the Android applications developed, using liuvc and libusb C/C++ dynamic libraries, [51, 52].

The main features of the CameraApp developed are:

- Streaming UVC-Compliant Cameras images.
- Capture of still images.
- Burst Capture of still images, allowing the user to select how many pictures to take.
- Image processing features for the low-level control of the camera settings
- Provided user control for ATMega2560 board.

The usability tests, as well as a full description of the CameraApp, will be described in Section 5.2.

4.2.2 Internal Fixation Point Actuators

It has been studied that a still fundus image of one specific area of the fundus may not be enough to evaluate if the patient under examination has DR or not, given a wide part of the fundus won't be covered in just one examination [25].

Additionally, a good fundus photography involves a steady image, where the most important eye structures for DR assessment are well visible for a correct diagnosis. For this to be possible, many fundus photography devices have integrated External, Internal or both, Fixation Targets, that consist on light points at specific locations, that the patient is asked to look at.

In the scope of EFS, the CameraApp developed in this thesis should establish the simultaneous control of the UVC-Compliant cameras and fixation point actuators, that serve this two purposes.

External Fixation Targets are located, as the name indicates, outside the imaging device used for FP [53]. For this reason, the system will be less compact and the risk of breaking this target is high. The solution for this problem are Internal Fixation Targets, fixated inside the imaging system.

Internal Fixation Targets main goal is to create a visual target, so that the person under examination can direct its gaze at that point, for an extended period of time [54]. Besides, this points will allow a very important feature, by having several targets to fixate, at different and very specific positions, several photographs of different regions of the eye can be captured, and can be integrated in a single shot, by *Stitching* technique, thus providing a wider FOV for examination.

Stitching consists on overlapping images taken from different angles of the fundus. At the moment, EFS can already use this technique for, as can be seen in Figure 4.4 [3].

Prior to this work, Melo, D. designed a possible optical system, for the integration of the Internal Fixation Points in the EFS Prototype, Figure 4.5. The LED matrix for

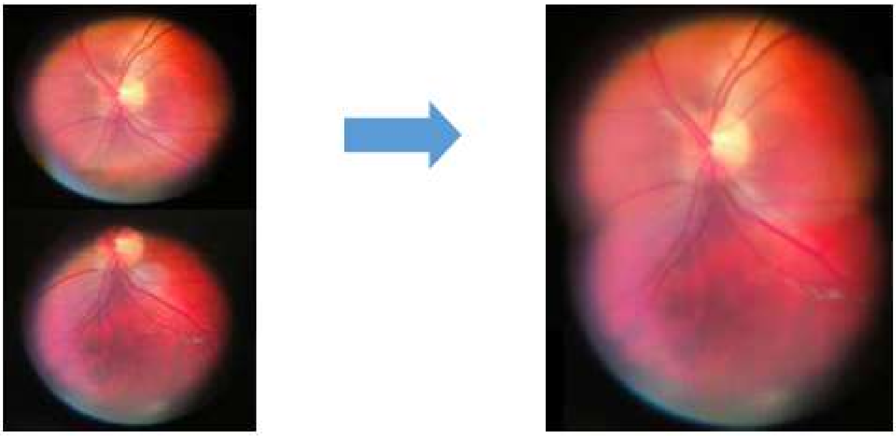
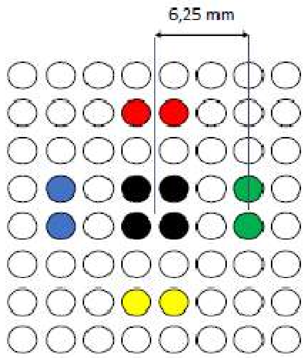


Figure 4.4: Fundus Images stitched together, providing a wider FOV of the retina, for DR assessment. Pictures obtained with the EFS prototype [3].

prototype integration was selected based on size and LED color, given the reduced size of the prototype [3].



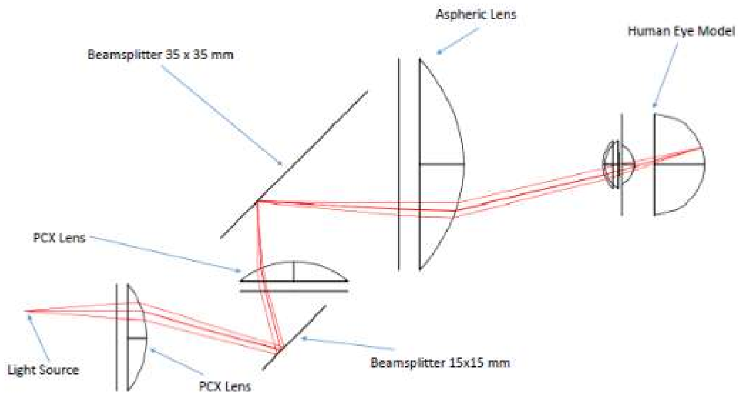


Figure 4.5: *(Left)* LED matrix, with the positions selected for the Internal Fixation Point Actuators in EFS: 4 Central LEDs and four pairs of periphery LEDs, for Top, Left, Right and Bottom positions. *(Right)* Internal Fixation Points Simulation for the Adafruit LED matrix , on the left. The points are being focused on the retina and the simulation was made using BEAM IV [3].

The model shown on the right side of Figure 4.5, is a test representation of one of the lateral fixation targets being focused on the retina. In this case, the light isn't centered with the optical path. It's the proximity with the retina that allows the patient to see the fixation targets, therefore this was the only requirement for the BEAM IV Display Path simulation. Since the optical system is roundly symmetrical, all rays equally deviated from the center will show the exact same behavior, therefore only one simulation was made, using, as mentioned, the central fixation targets [3].

The approach followed for the creation of the Internal Fixation Point Actuators in the EFS prototype started by establishing the communication between Android smartphones and an Arduino Mega 2560 microcontroller, based on ATmega2560 board, with 54 digital input/output pins. The board is connected to a Breadboard with a LED Matrix, an IR LED and a White LED, with integrated electronics.

Solution implementation required a BreadBoard with the following electronics:

- LuckyLight M1610008 KWM-2082CUB (Adafruit LED Matrix) [55]
- MAX7219CNG LED matrix/Digit display driver [56]
- 3 220Ω Resistors
- 1 μF (160V) Capacitor
- 10 μF (50V) Capacitor
- 1 ATmega5260 microncontroller board [57]
- 1 IR LED
- 1 White LED
- USB hub
- USB OTG converter cable

The BreadBoard setup, for the LED matrix, white and IR Led control, using the Adafruit Digital display driver, was made accordingly to the schematics in Figure 4.6, provided by Arduino [1] and Adafruit [2] manufacturers [58, 59].

[1] https://www.arduino.cc/

[2] https://www.adafruit.com/

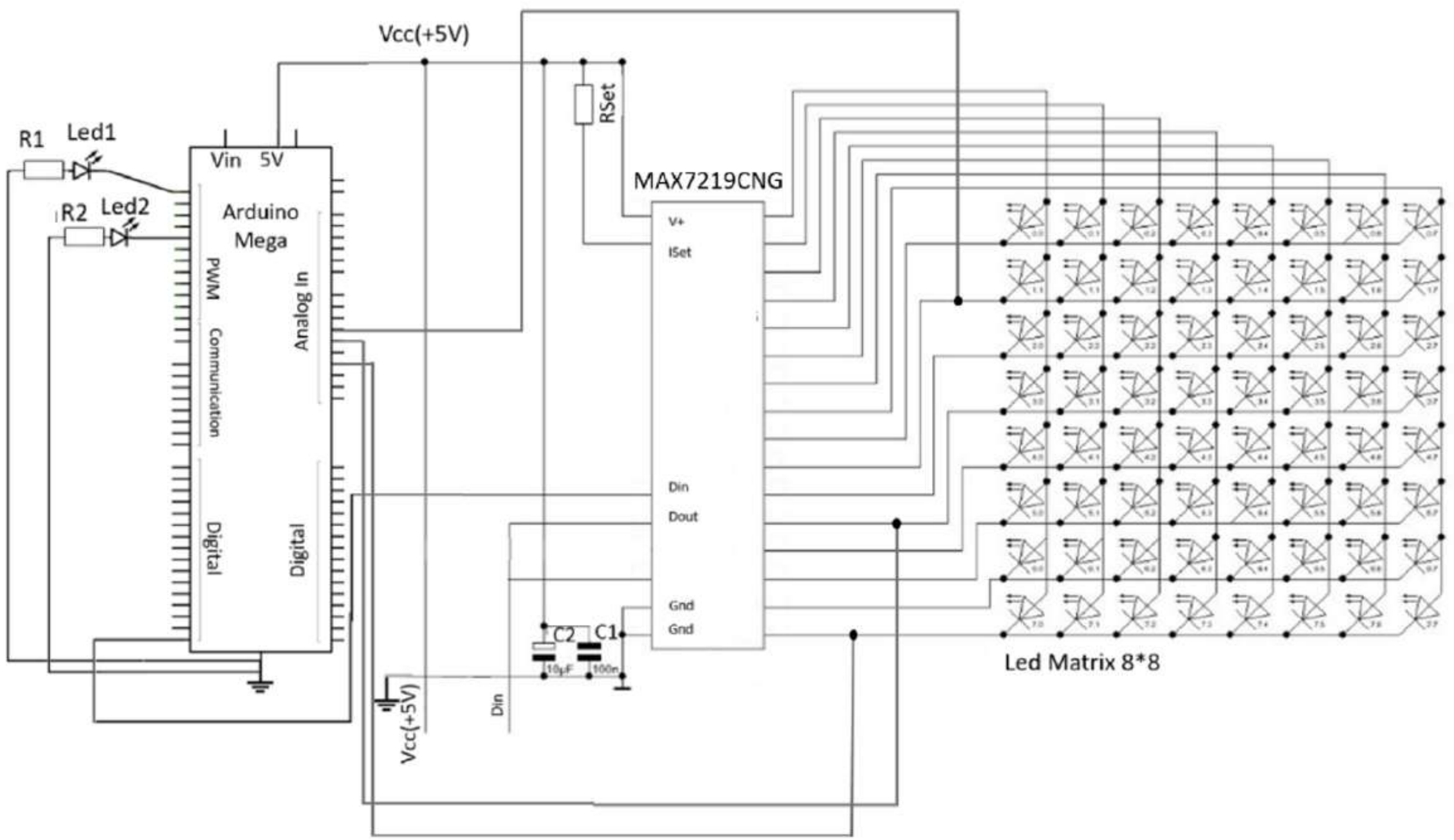


Figure 4.6: Complete Schematics for control of the 8*8 Led Matrix and white and IR LEDs, represented by Led1 and Led2. Adafruit MAX7219CNG Digital display driver was used for the LED matrix control, along with one 220Ω Resistor, and two Capacitors with 1µF and 10µF. For the white and IR LEDs, two Resistors, R1 and R2 were used, both of 220Ω. Arduino Mega Board was employed to control the LEDs display. Adapted from [59, 60].

In this thesis, a Communication and Acquisition Protocol was integrated in the *CameraApp* Android Application developed, so that the user can control image capture with the UVC-Compliant Camera simultaneously to displaying the stream video image and controlling the Internal Fixation Target actuators.

4.2.3 CameraApp: Still Image Capabilities

DR Imaging systems need to be tested so that its quality is guaranteed to the detection of DR structures. Quality tests are divided in three categories, as described in Table 4.1.

Table 4.1: System tests for evaluation of factors that affect the quality of fundus images. Adapted from [61].

Optical Properties	- Illumination - Light scatter - Pupil Size Requirements - Retinal FOV
Image File Properties	- Resolution - Color Depth - Image file type and size
User Properties	- Alignment - Computer-user interface - Information system interface - Ergonomics

Illumination is required in low-light environments, as is the case of the human fundus. EFS has an illuminations system constituted by a white and IR LED. The protocol established in this thesis, allows the control of this LEDs, that in this specific case are integrated in the BreadBoard for the Internal Fixation Targets, controlled by an ATmega2560 board. Light Scatter and Pupil Size Requirements were studied by Melo, D., that established the minimum pupil size, without dilation, to be 4mm [3].

Retinal FOV measurements, further described in Subsection 5.2.1, include an optical setup constituted by the cameras selected for integration in the prototype, a 35mm PCX Lens, millimeter paper and a Nexus 5X smartphone, that is used in the current version of EFS, for a possible comparison of the outcomes obtained with the two solutions.

Image file properties should demonstrate the quality of the image in terms of Resolution and Color Depth. Resolution is defined as an image system's ability to distinguish object details, and it's often expressed in terms of line-pairs per millimeter. A low resolution image usually lacks fine-detail and is often blurry, whereas a high resolution image is highly detailed and clear [62].

Color depth determines the true color balance or optical density of any color rendition system.

Aliasing is also a common issue in photography. It is an artifact created by the presence of frequencies in the image that are too high when compared to the sensor's sampling frequency [63].

Image colors can also be accessed, since there can be some undesired color saturation. This issue refers to the brilliance or purity of a color. When the colors present in an image are projected at the proper screen brightness and without interference from stray light, or are printed at high output resolution, saturated colors appear bright, deep, rich and undiluted [63].

Wavelength influences the performance of the optical system, given different wave lengths bend at different angles as light passes through a certain medium. Shorter wavelengths are bent more then longer ones, creating problems for the imaging system, when trying to resolve details and gain information [19].

Chromatic aberrations are usually of two types, lateral color shift and chromatic color shift, Figure 4.7. The first type, referring to lateral color shift can be seen when the center of the image is moved towards the edge of the image. In the center, concentric wavelengths of light spots will appear. At the borders of the image, these wavelengths tend to separate and produce a rainbow effect. As a result of this color separation, a given point on the object is imaged over a larger area, resulting in reduced contrast, a result that affects sensors with smaller pixels in a more pronounced way, since the blurring spreads over more pixels [19].

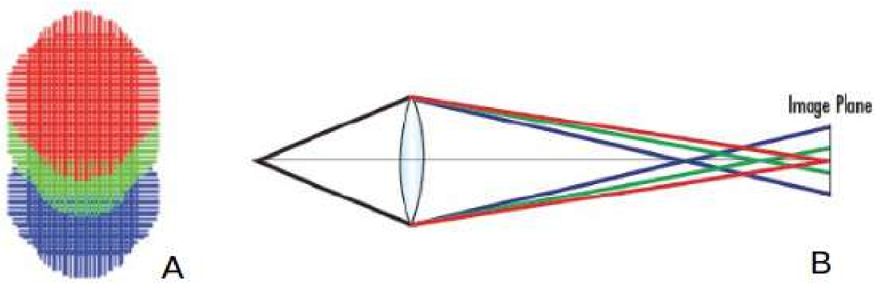


Figure 4.7: Types of chromatic aberrations: A-Lateral color shift, B- Chromatic color shift. Adapted from [19].

The second type of chromatic aberration is chromatic color shift, relating the ability of a lens to focus all wavelengths at the same distance from the lens. Different wavelengths will have different planes of best focus. This effect also results in reduced contrast, since different wavelengths create different size spots at the image plane where the camera sensor is located [19].

If the optical system is not completely aligned, there is a great probability of the existence of chromatic aberrations, usually of the lateral color shift type, since the image won't be completely focused in one plane.

Image format is important in terms of saving data storage space on the smartphone, but always guaranteeing a high-quality image file. There are several formats for saving images in mobile devices, but the ones that are based on lossless compression, as Portable Network Graphic (PNG) format, have the advantage of assuring this relation between quality and space saving, thus constituting a good option for medical imaging devices [64].

Given this reason, this is the privileged image format for saving fundus images in the work developed.

The alignment of the system depends on many factors, including the optics system and the camera position, thus to reach the best outcome, the camera selected in this work for integration in the EFS prototype, should be set inside the optical system, integrated with the lenses and beamsplitter that are responsible for the refraction and reflection of light that allows the system to photograph the human fundus.

The computer-user interface and the information system interface, described in Subsections 5.2 and 5.3 offer an information tool, so that the user can quickly comprehend how to use the Internal Fixation Targets. This tool fully describes how the protocols for targets control are established, thus constitute an important feature of the CameraApp, since it eases the use of the Computer-user interface and thus ensures that it is ergonomic.

CHAPTER 5

Results

5.1 Cameras Selected in the Scope of EyeFundusScope

In Section 4.1, several types of cameras were evaluated for integration in the EFS prototype. Given the reasons presented in Section 4.1, UVC-Compliant Cameras were selected for this thesis. Still, a wide range of options is available within this category, therefore, after researching several solutions, Table 5.1 shows the three cameras selected.

Table 5.1: Camera Selection by Camera Specifications. *Label.* NA - Not Available, A* - Available by customization.

Parameters	Logitech C270 webcamera [45]	Ascella (See3CAM_CX3ISPRDK) [65]	e-CAM51_USB [66]
Sensor Type	-	OmniVision OV13850 (CMOS)	OmniVision 5640 (CMOS)
AFOV	60º	70º	60º
Resolution	3.0MP	13.0MP	5MP
Dynamic Range	-	HDR	68 dB
No Infra Red Filter (NoIR)	NA	NA	A*
USB Connection	2.0	2.0/3.0	2.0
Price	$21.50-$35	$299	$89

The parameters described in Table 5.1 were the deciding factors for the camera selection. Based on what was said in section 2.4:

- CMOS sensors are smaller and very versatile, constituting a good choice for integration in the small dimension prototype.

- The AFOV for an approximate 40º FOV value, that is desired for a DR assessment systems, should be around 50º to 60º.
- Camera resolution should have at least 5MP, as defined by *ISO 10940:2009* norm [15]. This value was obtained based on the requirements of minimum separation of two adjacent lines on the fundus (number of line pairs per millimetre) and the distance between two pixels (from center to center) of a digital image sensor theoretically projected on to the fundus.
- Cameras without IR filters are good options for capturing images with low frequencies, like the ones captured in low-light conditions, as is the case of fundus pictures.
- Preferentially, the USB connection should have the option to be 3.0, since it allows a faster connection, thus displaying an almost immediate stream video.
- The price of the selected camera should not add relevant costs to the prototype.

It was very difficult to find a camera with all this features, therefore, the three cameras in Table 5.1 were selected, since all of them are better at at least one characteristic then the other, and they are all UVC-Compliant, thus they would be compatible with the Android System developed, and that would facilitate its testing.

Logitech C270 webcamera was selected since it was a very cheap device, with a FOV within the required values, despite having a very low resolution, only 3MP. The main goal of testing this camera was to see if the Android System developed could actually stream video and simultaneously capture images from an UVC-Compliant Camera, and it proved to be useful for this task.

The Ascella (See3CAM_CX3ISPRDK) Camera is a more sophisticated camera, of high-resolution (13MP), with a USB3.0 connection and a High Dynamic Range (HDR), but its FOV is slightly higher then the one required for EFS, it doesn't allow capture without IR light source filtering and it is a very expensive camera.

The last option was the e-CAM51_USB UVC-Compliant Camera Module, that combined this last two in terms of having a 60º FOV, that's within the required range, a 5MP resolution, the option to take pictures without IR filters and being relatively cumbersome. The less positive points of this camera is the USB 2.0 connection. Given delays in the delivery of this camera by the manufacturers, it could not be implemented in the duration of the thesis.

5.2 Android Camera Application: UVC-Compliant Cameras

In order to test the correct functioning of the CameraApp application created, the two cameras selected in Section 5.1, Ascella (See3CAM_CX3ISPRDK) and Logitech C270, were connected, separately, to an Android Smartphone, using the respective camera vendor USB connection cable and an USB OTG cable, as represented in Figure 5.1. Two

Android Smartphones (Samsung A3 2016 and Samsung S5) were tested, and are fully compliant with the application.

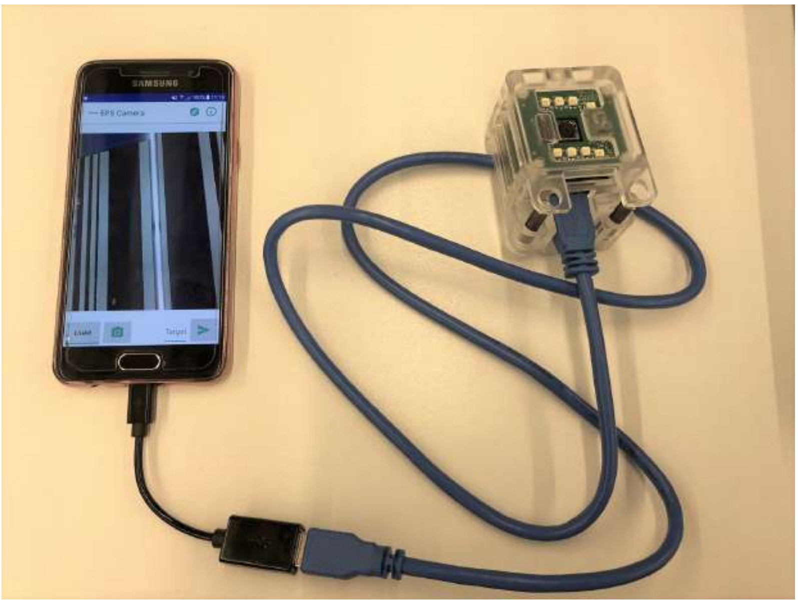


Figure 5.1: Montage used for testing the usability of CameraApp. An Ascella (See3CAM_CX3ISPRDK) Camera, with an USB3.0 Type-A to Micro-B cable *(in blue)* was used, as well as an USB OTG cable *(in black)*. This last one was then connected to the micro-USB port of a Samsung A3 2016 smartphone.

Once the camera is connected to the CameraApp application, the User must grant the necessary permissions to enable it. This is a security measurement necessary in Android systems, Figure 5.2. Once those permissions have been granted, the image stream will be available in the smartphone screen, as well as user interaction functions for image capture, burst image capture and image processing settings.

The image capture can be made in two modes, as mentioned, the single capture and burst capture mode. These are both available by clicking the capture button, displayed in the CameraApp application, while the stream video is active.

For the single capture mode, the user clicks on the capture button only once, and the image is saved to the *EyeFundusScope* folder, created in the internal memory of the smartphone. The first time this process occurs, permission to write to external storage needs to be granted by the user, thus a new message appears, in a similar way to the ones shown in Figure 5.2 *A* and *B*.

If the user wishes to take several pictures at once, burst mode should be more effective. One long click of the capture button will display an Android *DialogFragment* that allows the selection of the amount of pictures to save to the *EyeFundusScope* folder, as shown in Figure 5.3.

The images are saved in the PNG image format, since it supports lossless compression, that is in accordance with what was described in Subsection 4.2.3.

For the smartphone used in this tesis, Samsung A3 2016, the resolution of the saved

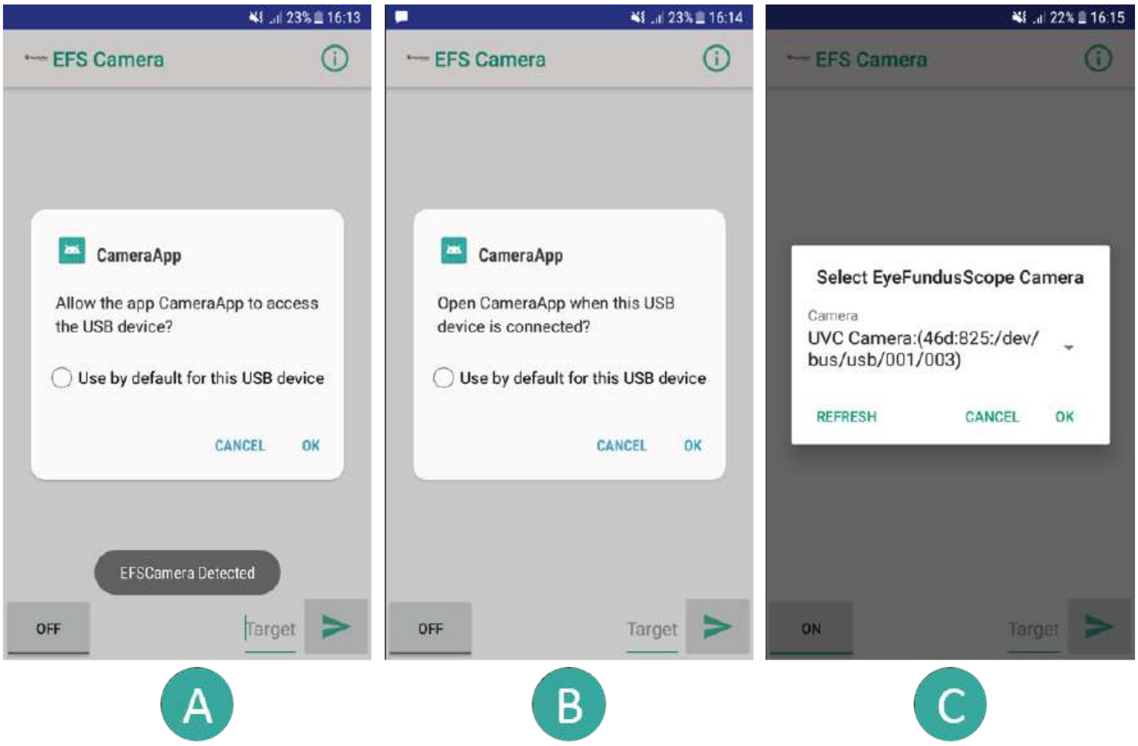


Figure 5.2: CameraApp application.*A* and *B* show the permissions required for the application to access the connected USB device. Once those are granted, message *C* specifies the UVC Camera to stream video from. Settings and Capture buttons are now available.

images was 720 x 600 px, because the screen width of this smartphone is 720px. If the CameraApp is used on another smartphone, with a wider or more narrow screen, then this value changes, adapting to the new width.

Finally, the low-level control of the camera's characteristics was one of the objectives of this thesis, that should evaluate the possibility for such level of control. This proved to be possible, and image processing can be done to the stream video while it's being displayed, as well as save those changes in the captured image. Figure 5.4 exemplifies the features that can be changed by the user.

Fundus images are captured, as has been said, in low-light environments, causing EFS prototype to capture images using a white-light LED flash to properly illuminate the fundus, so that an image can be captured by the system.

This illumination module leads undesired color changes in the fundus photography, causing it to be heavily weighted towards a yellow-red tonality. This causes retinal pigmentation and blood vessels to look exaggerated in the captured image. To reach color accuracy, White-balance mode should be applied to match the spectral characteristics of the illumination source [64].

The color balance is achieved by altering the relationship of the RGB color code of the image pixels. Since in this work the fundus image obtained will appear with the yellow-red tonality described, a cooler temperature white-balance mode must be applied,

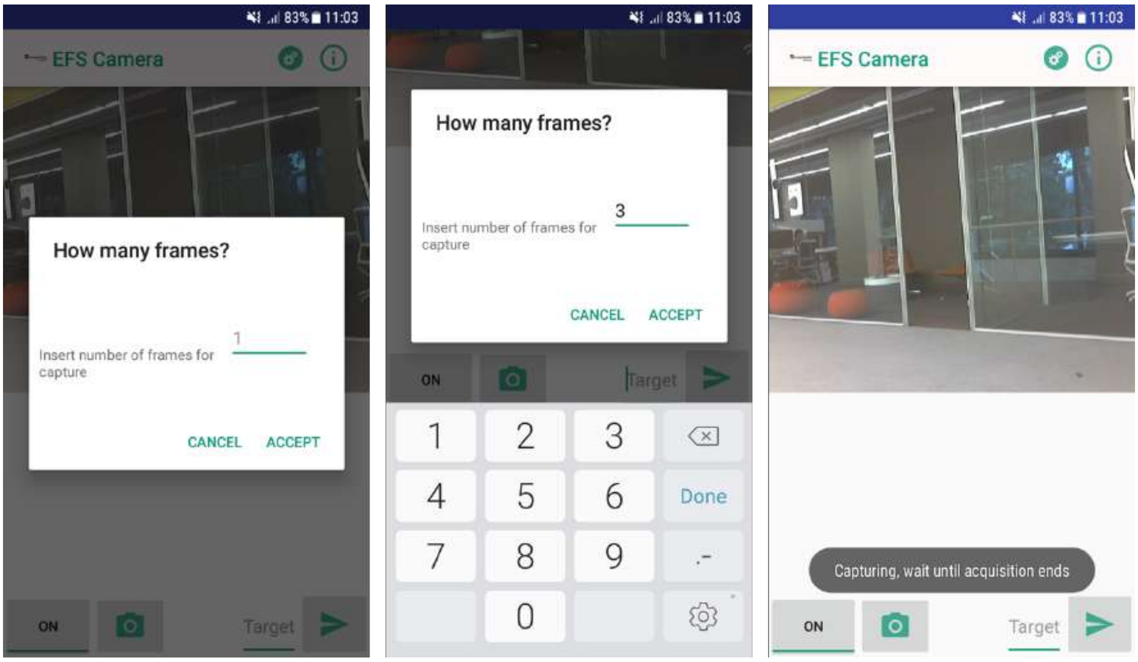


Figure 5.3: CameraApp burst capture mode. The capture button at the right of the camera's *ON/OFF* button, must be pressed for a few seconds, in order to show the frames selection *DialogFragment* (central image). While the *Capturing* message is being displayed, the user needs to keep the prototype focused and immobile for capturing.

since this will match the lightning conditions, thus originating an image closer to reality [64].

CameraApp application features include the control of the white-balance mode, and for the conditions described during acquisition, the user should change the colors to the first mode in Figure 5.5, that were obtained with Logitech C270 webcamera, using CameraApp.

Another important low-level control of the camera sensor for EFS is the ISO value. Changing this value will brighten or darken the photograph, which is a good tool for images taken on dark environments. To fully adjust the ISO value, settings like shutter speed, that controls the amount of light that enters the sensor, should be evaluated, but at this moment CameraApp can only adjust the brightness value of the stream video/captured image.

Auto-Focus is automatically enabled for UVC-Compliant Cameras that support it, as is the case of the Ascella (See3CAM_CX3ISPRDK) Camera, but sometimes, given the close proximity of the camera to the optical path lenses, focusing the image automatically results in slightly blurred images. To solve this issue, CameraApp can disable the focus mode, and it can be adjusted manually by the user.

Contrast describes the separation, in intensity between black and white pixels. This feature is important in terms of image resolution, helping define image details [67]. This is also important for EFS, specially in the detection of some of DR characteristics, such as exudates or hemorrhages, that in early stages are not as noticeable without contrast

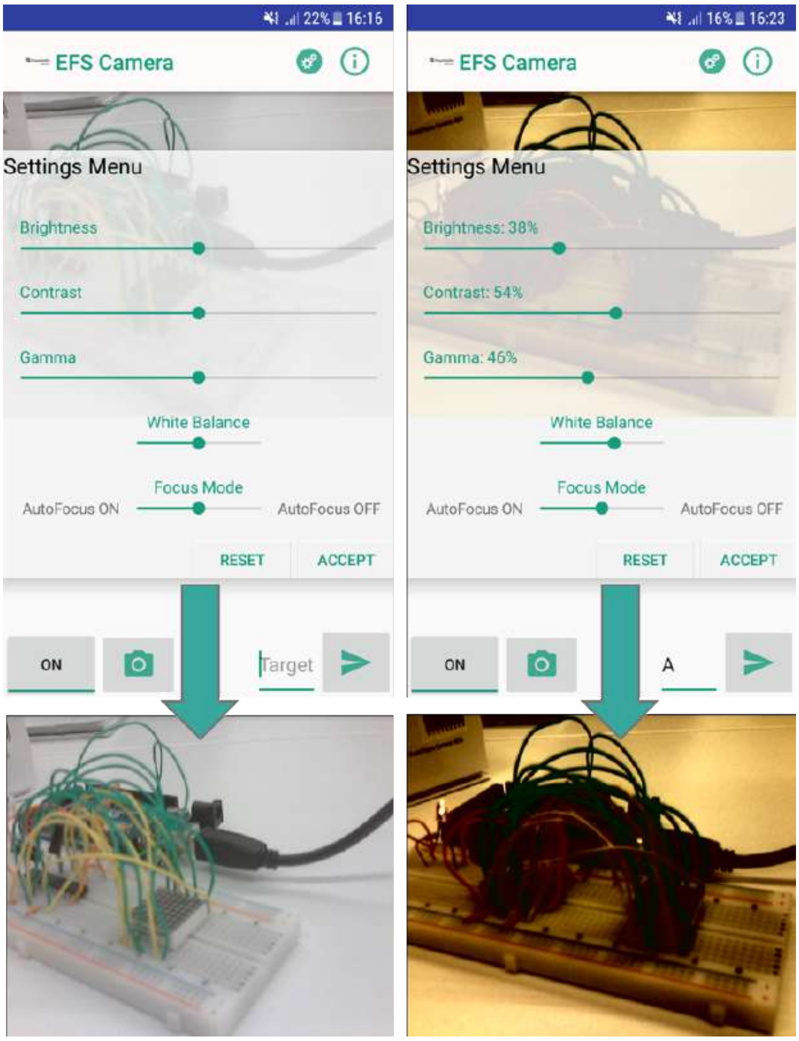


Figure 5.4: Example of low-level control of the camera - Image processing. By clicking the Settings Button, on CameraApp *Toolbar*, The parameters displayed in the central image can be changed for a better image capture/display.

Figure 5.5: CameraApp has a white-balance controllable feature, that can be adjusted by the user before image capture, by adjusting the value of the white-balance *Scrollbar* implemented in the Settings Menu.

adjustment.

The last adjustable feature in CameraApp is the Gamma Correction, that defines the relationship between a pixel's actual luminous intensity and it's numerical value. The human eye is very perceptive to changes in dark colors, but camera's do not function exactly like that, thus this parameters needs to be adjusted, in order to relate the camera's and the human eye light sensitivity [68].

Given the two UVC-Compliant Cameras selected (Section 5.1 are working as expected, displaying a video stream while taking pictures of the fundus, it is expected that all cameras, even future ones, that are still not available in the market, are fully compliant with the Interface created, provided the Vendor-ID number of the device is known.

In 2005, there were twenty-six vendors with UVC-Compliant Products, number that seems to be rising. This proves to be a very good feature for this application, since the interface created won't require time consuming changes to fully integrate a different UVC-Compliant camera that emerges in the market, with better features for EFS's Optical System [69].

Adding an UVC-Compliant camera to EFS has clear advantages as the maintenance of the optical alignment of the system, and the image characteristics, despite the Android Smartphone being used, but the low-level control of the camera is also very important. Table 5.2 establishes the comparison between the controllable parameters for both cameras, in order to evaluate if the requirements for taking a photograph of the human fundus can be fulfilled by both.

Table 5.2: CameraApp and Enhanced Camera API low-level controllable parameters comparison.

Low-Level Parameters	CameraApp: UVC-Complian Cameras	Smartphone Cameras
Brightness	Yes	Yes
ISO	No	Yes
Contrast	Yes	Yes
Shutter-Speed	No	Yes
Gama	Yes	Yes
White-Balance	Yes	Yes
Auto-Focus/Manual-Focus	Yes	Yes
Manual-Focus	Yes	Yes

Despite not being able to control ISO and Shutter-Speed, due to limitations of the libraries used in the development of CameraApp, the application can already manage to alter many other image settings. This way, it was proved in this work that it is possible to control low-level camera parameters relevant for the capture of such images, but there is still work to be done in this field.

It is also important to refer that the settings on Table 5.2 only work on cameras that posses such parameters, thus it's important, when selecting an UVC-Compliant camera, in case of CameraApp, or a smartphone, for Enhanced Camera API, that this features are evaluated.

5.2.1 Field-of-View Prototype Results

The usability of the CameraApp developed in this thesis, as well as the capabilities of the resulting imaging path were tested in the Optics Instrumentation Laboratoty of Faculdade de Ciências e Tecnologias - NOVA University of Lisbon. A montage, as the one seen in Figure 5.6 was used, being constituted by the following components:

- Optical Post Holders.
- Optics Table.
- Millimeter paper.
- 35mm PCX Lens.
- EFS prototype (constituted by 3D printing prototype and several lenses for light refraction and optical alignment).
- Samsung A3 2016 Smartphone.
- Logitech C270 webcamera, with a 3D printed support.
- Ascella (See3CAM_CX3ISPRDK) Camera.
- Right Stand support.
- Three Prong Extension Clamp.
- USB OTG cable [70].
- USB 2.0 camera cables (from the respective vendors).

The Optical Table, Optical Post Holders, the 3D printed support and Right Stand support mounted with a Three Prong Extension Clamp helped with the systems Optical Alignment, keeping the PCX lens, the millimeter paper and the respective UVC-Compliant cameras in place for the acquisition tests.

The millimeter paper had the main purpose of replacing the retina, where the image is formed, since it is a graduated target, that facilitates the measurement of the FOV. A 35 mm focal PCX lens was placed at the end of the EFS prototype to replace the eye's refractive center, and the two UVC-Compliant Cameras, Logitech C270 webcamera and Ascella (See3CAM_CX3ISPRDK) Camera, were placed at the right of the final prototype lens, one at a time, and they were connected to the smartphone using the USB OTG and the respective USB 2.0 camera cables.

The millimeter paper was aligned so that it would be centered and perpendicular to the optical axis, but given the EFS prototype was used as the optical path for light reflection and refraction, and since it can't be fixated to the Optics Table, it was difficult to do this exactly, thus the resulting images are not completely centered.

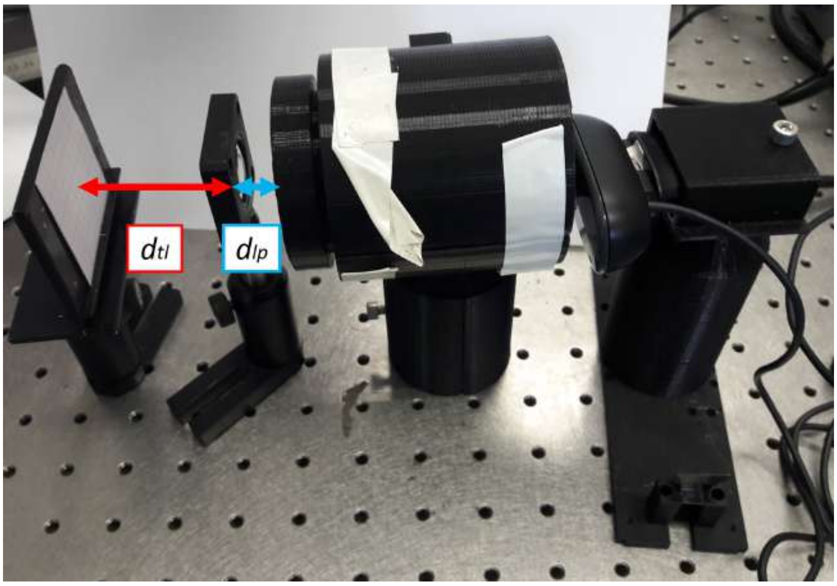


Figure 5.6: Montage used for obtaining the FOV of the optical system. The distance from the millimeter paper and the PCX lens is given by *dtl* and *dlp* is the distance from the PCX lens and the EFS prototype end. The camera used alternated between the two UVC-Compliant cameras tested and the Nexus 5X smartphone camera. For the setup presented in this image, Logitech C270 webcamera was used, as close to the prototype as possible. For the final tests presented in this work *dtl*=50mm and *dlp*=0mm, instead of the distances represented in this figure.

As mentioned in Section 5.1, Table 5.3 resumes the AFOV values of the three tested cameras, so that conclusions about the FOV of each camera can be established. The EFS prototype was dimensioned specifically for the Nexus 5X smartphone camera, that according to its specifications [71], has a 4.54mm width sensor and a 4mm focal length. This way, the Nexus 5X AFOV was calculated, according to equation 5.1, resulting in an approximately 60º AFOV value.

$$AFOV(rad) = 2 * tan^{-1}(0.5 * \frac{4.54mm}{4mm}) \leftrightarrow AFOV(rad) = 1.032rad \rightarrow AFOV = 59.14^{o} \quad (5.1)$$

Table 5.3: AFOV values of the three cameras tested, [42, 45].

	Logitech C270 webcamera	Ascella (See3CAM_CX3ISPRDK) camera	Nexus 5X camera
AFOV	60º	70º	60º

The results obtained for the FOV calculation, with the two UVC-Compliant cameras are shown in Figure 5.7. Another test, using the same configuration, was performed with the Nexus 5X smartphone, for comparison with the results of the cameras studied as possible to integrate in the EFS prototype, Figure 5.8.

The mounting configuration of the EFS prototype and the Nexus 5X smartphone was different from the two UVC-Compliant cameras. For maintaining the optical alignment, the Nexus 5X smartphone must be placed in a specific cover, as shown by the scheme in Figure 3.6, that sets the distance between the smartphone camera and the prototype lens at 20mm.

The UVC-Compliant cameras were set as close as possible to that same lens, using a montage similar to the one presented in Figure 5.6. The distances d_{tl}=50mm and d_{lp}=0mm, were the same for all three tests. Nexus 5X smartphone and Ascella images were obtained using AutoFocus feature and Logitech C270 webcamera image with fixed focus, since it doesn't support AutoFocus mode.

The light conditions were also different between the UVC-Compliant Cameras and the Nexus 5X smartphone, since this last one used a white-Led as illumination source for image acquisition. As has been said, the CameraApp developed in this work also allows the control of a white-Led, with the same purpose, but this Led is still on the board for the internal fixation point actuators, since its purpose it's to be controlled simultaneously with this points for the capture of a wider fundus. Since the board has not yet been integrated inside the prototype, the images for this two cameras were obtained only with the room's natural light, thus resulting in darker images then the one obtained with the Nexus 5X, as is visible on images 5.7 and 5.8.

In order to calculate the FOV, the distance *2r* was measured, from edge to edge on the image of the visible scale, set by the millimeter paper. The FOV calculations followed equation 2.2, and the results for the Logitech C270 webcamera and Ascella (See3CAM_CX3ISPRDK) are displayed in Figure 5.7.

The FOV for the three images was calculated based on Equation 5.2, being $X_{distance}$ the distance in any direction between the center and the circumference limiting the observable area and d_{tl} is the distance between the refractive center, represented here by the PCX lens, and the target in the millimeter paper.

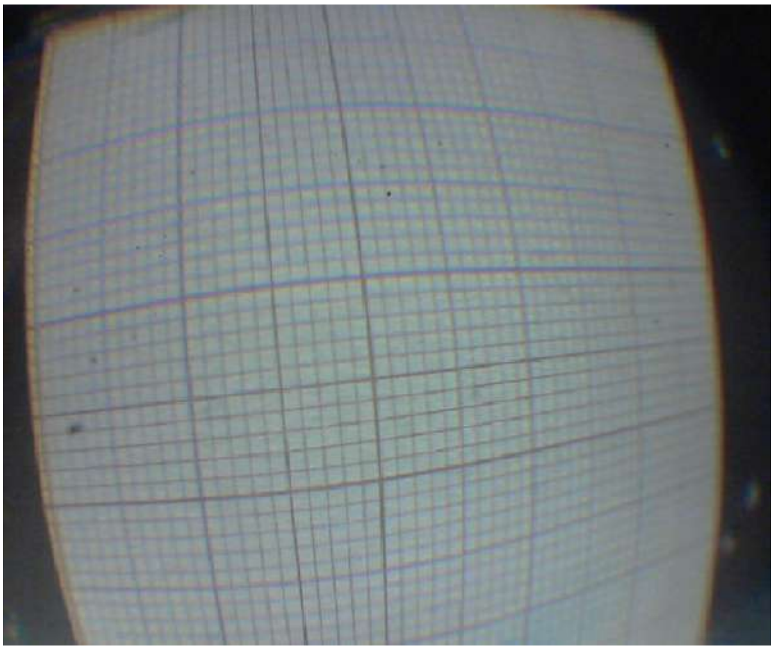
$$FOV(^o) = 2 * tan^{-1}(\frac{X_{distance}}{d_{tl}}) \tag{5.2}$$

FOV results with Logitech C270 webcamera, Figure 5.7a:

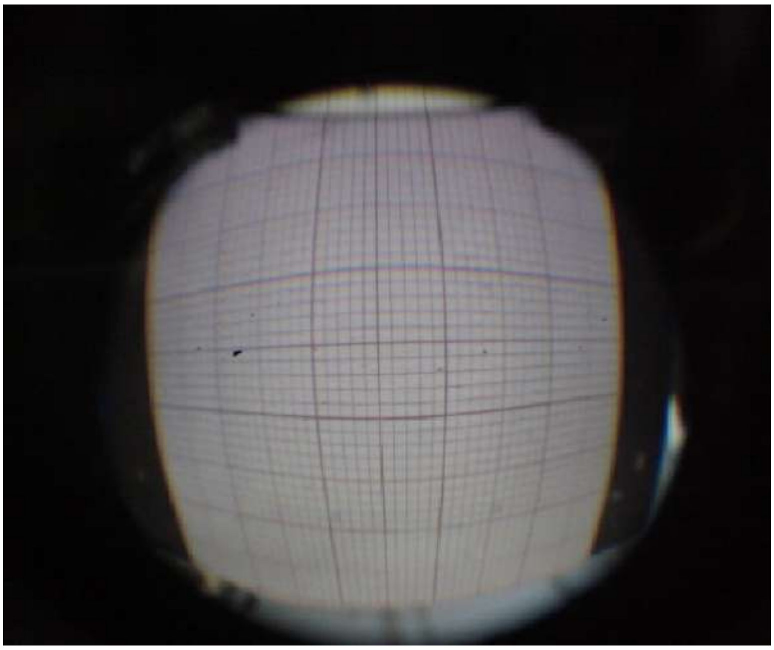
$$FOV(^o) = 2 * tan^{-1}(\frac{31mm}{50mm}) \Leftrightarrow FOV(^o) = 63.60^o \tag{5.3}$$

FOV results with Ascella (See3CAM_CX3ISPRDK) Camera, Figure 5.7b:

$$FOV(^o) = 2 * tan^{-1}(\frac{26mm}{50mm}) \Leftrightarrow FOV(^o) = 54.94^o \tag{5.4}$$



a Millimeter paper photography using Logitech C270 webcamera



b Millimeter paper photography using Ascella (See3CAM_CX3ISPRDK).

Figure 5.7: Results obtained with Logitech and Ascella (See3CAM_CX3ISPRDK) Cameras, with the montage in Figure 5.6. The FOV values were obtained by measuring the visible area, and using equation 5.2.

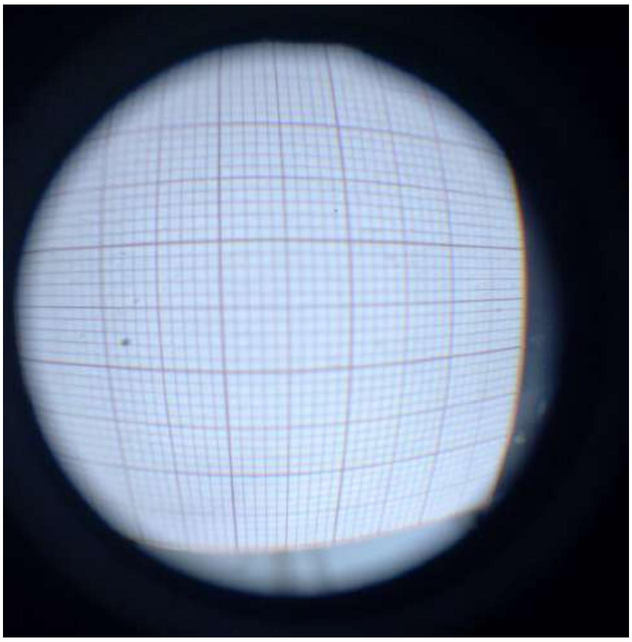


Figure 5.8: Results obtained with Nexus 5X smartphone camera, with the montage in Figure 5.6.

FOV results with Nexus 5X smartphone Camera, Figure 5.8:

$$FOV(^o) = 2 * tan^{-1}(\frac{24mm}{50mm}) \Leftrightarrow FOV(^o) = 51.28^o \tag{5.5}$$

Due to the distance between the prototype lens and the cameras, even though the Logitech C270 has a 60º AFOV, that is the same value of the Nexus 5X smartphone AFOV, the final FOV, calculated in Equations 5.3 and 5.5 differ from one another in about 11º, resulting in a cropped image and a wider FOV for the Logitech C270 webcamera. This should be solved if the webcamera were set at about 20mm further from the prototype lens, as it happens with the Nexus 5X camera.

Through equation 5.4, it was possible to obtain the FOV for the camera Ascella (See3CAM_CX3ISPRDK), that is 54.64º. This value is slightly higher then the Nexus 5X smartphone camera FOV, as expected, since the AFOV of this camera is 70º, being 10º larger then the Nexus 5X AFOV.

Due to this difference, in Figure 5.7b, it's possible to see, on top of the image, a line and a small dark square. These constitute the *beamsplitter*, used for the diffraction of the light rays to obtain the final image. If in the future, this camera is fully integrated in the EFS prototype, some changes to the optical system are required in order to suppress this issue.

The image analysis evaluated the existence of aberrations qualitatively, since there were no methods available for a quantitative analysis. The images obtained in Figure 5.7 are very clear, demonstrating that there are no undesired reflections that could cause problems in DR diagnosis, since these can cover some important parts of the fundus.

A small percentage of *aliasing* was detected, that is demonstrated by the blur closest to the periphery of the millimeter paper. This characteristic is normal, since the prototype lenses are curve, given the fundus of the human eye is also curve. Since the millimeter paper used for the tests was set in a plain surface, some *aliasing* was expected, that is completely disappears when the photographed surface as a round shape. This can be confirmed by Figure 5.9, taken using EFS prototype with the Nexus 5X smartphone camera, to an eye model.

Figure 5.9: Eye phantom model image captured using Nexus 5X smartphone and the current EFS optical system prototype. Aliasing is very reduced when comparing to the plain millimeter paper images captured, despite revealing some chromatic aberrations closest to the borders of the eye model.

5.3 Android Camera Application: Internal Fixation Targets

The capture of a fundus image is done at low-light environment conditions, thus the need to use an IR LED, to allow the streaming of the fundus image without requiring the use of a white LED that can damage the eye if used for a long period of time, at a very close distance. For this reason, the IR LED is turned ON at the same time as the matrix LED's, on the different acquisition positions. The white LED is used to capture the image, thus it is light ON when both the IR LED and the matrix LED's are turned OFF.

Since the image needs to be well centered, in order for the outcome to be the best possible, the person that is handling the EFS prototype will have to hold it in front of the patient's eye, and move it closer or further away from it, until the image that appears on the screen is well focused and the desired regions of the eye are in display.

This way, two modes are available in the UI, as seen in Figure 5.10:

- Testing mode

- Acquisition mode

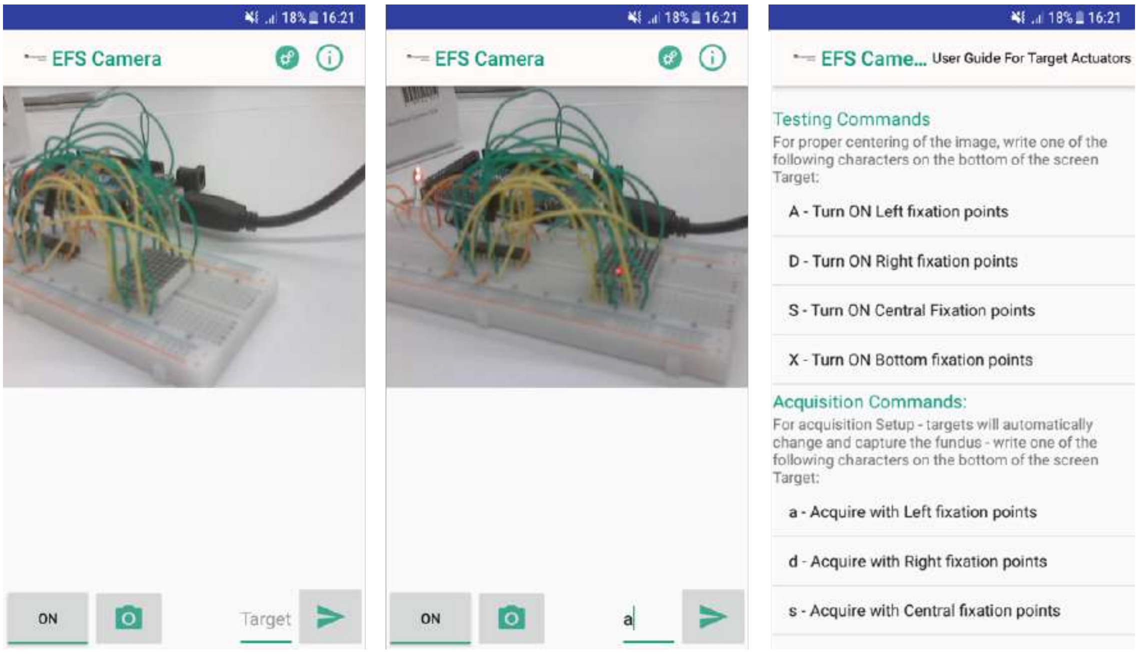


Figure 5.10: CameraApp has control over the ATmega2560 board in order to light ON/OFF the LED matrix, IR-light and white-light LEDs for acquisition. This is done by writing specific commands, described at the User Guide, in an Android *EditText* box, identified as "Target". ***Left image:*** No Targets selected, the matrix LEDs are OFF. ***Center image:*** The user selected Target "*a*", turning ON the Acquisition mode for Left Fixation Points. ***Right image:*** User Guide to assist the user in the selection of the Target Actuators.

These two modes are very similar, working under the same principle. In the Android Application, there is an *Handler* that converts the message sent through the form of a String into an Arduino *Char (single character)* Command. The characters are defined in an Arduino IDE *.ino* file, and they define the way the matrix LED's are turned ON/OFF, as well as the way the IR LED and White LED are displayed.

For the Testing mode, only the IR LED and the matrix LED's are used, since the aim of this mode is to assure that the fundus is well centered in the image display.

The Acquisition Mode is automatic and it must be used after Testing Mode, given this mode is automatic and runs on only 15 ms, the centering of the image will be very difficult for the user. It is important that the user keeps as still as possible during acquisition, so that the outcome is the best possible. The command sent in Acquisition Mode must be the capital letter of the one sent in Testing Mode, since these correspond to the same LED positions, differing only in the way the acquisition is set.

In this mode, all the LED's connected to the Breadboard are used, as explained before. The IR LED and the specified matrix LEDs will both be light ON during 5 seconds, so that the patient fixates the light of this last ones. After those 5 second, both the LED matrix and the IR LED are turned OFF, simultaneously with the white LED being turned ON.

This step is very quickly (15 ms), since we must consider the response time of the human eye, so that the patient doesn't lose focus of the fixation target.

As it was studied, the time that an average person takes to detect a change in a viewed image is around 12-15ms. This way, if a change in a given scenario occurs under this small interval of time, a observer won't notice any changes. For the case being studied, this means that when the process of turning the matrix LED ON and OFF, if the 12-15ms time is exceeded, the patient will notice that the red LED light is not in the same position, and there is a great chance that he loses track of the target.

Since the time interval referred is very small, it is likely that the captured image will require some image processing.

Chapter 6

Conclusions

Diabetic Retinopathy is a pathology that affects millions of people worldwide, being the leading cause of avoidable blindness for adults with working age. There already exist some mediums for DR diagnosis, but these are either too expensive, non-portable or not very accurate. This way, EyeFundusScope prototype was developed, being a handheld medical smartphone based imaging device for DR assessment. This prototype is currently uses the smartphone's camera for capturing the fundus image, but despite being a good solution, it still needed improvements, thus the four main objectives of this thesis were set:

- Research the use of dedicated camera boards, to use in the prototype developed by Fraunhofer.
- Evaluate the use of UVC compliant cameras, because they are natively supported by most operative systems.
- Establish a communication protocol to allow the Android smartphone to control the camera and to display a preview stream during capture.
- Define a protocol for data acquisition with actuators for internal fixation points.
- Develop an approach for low level (highly parametrized) control of high resolution and low cost camera modules.

The use of external cameras was evaluated in this thesis, reaching the conclusion that the best cameras to integrate in the EFS prototype should be UVC-Compliant cameras, given their easier integration in terms of not requiring specific drivers, being easily integrated based on the UVC-Protocol, being simple Plug&Play devices and their small size dimensions for prototyping.

The UVC-Compliant cameras selected for the prototype integration were Logitech C270, Ascella (See3CAM_CX3ISPRDK) and e-CAM51_USB cameras. This last one, was taught out to be the better choice amongst the three selected, given its characteristics, that include:

- 60º FOV, that's the same as the Nexus 5X smartphone used for the optical system developed. This would suppress the need for altering this system, since cameras with the same AFOV should produce images with the same FOV.
- 5MP Resolution, that is considered the minimum acceptable value for digital fundus cameras by *ISO 10940:2009* [15].
- Good results in capturing low-light environment photographs, given its NoIR functionality.
- Relatively low-price, given its features.

Despite this, due to vendor issues, it couldn't be delivered during the course of this thesis, thus only Logitech C270 and Ascella (See3CAM_CX3ISPRDK) cameras were tested.

In this work, an Android application, entitled CameraApp was developed, successfully establishing a communication protocol between Android and UVC Compliant devices, that constituted one of the main objectives of this work. This was accomplished by the implementation of methods established by [50–52] Open Source Libraries, that include the USB Video Class devices Protocol, for the control of cameras that support this driver.

CameraApp features include the video stream from the camera connected through the micro-USB port of the Android smartphone, with simultaneous capturing, as well as control over Internal Fixation Target Actuators for peripheral imaging, another objective of this thesis, that could be achieved.

The Internal Fixation Targets have the purpose to reduce patient eye movement, and therefore possible image artifacts, as well as enabling the capture of pictures of several angles of the retina, for posterior application of *stitching*, in image processing. This creates the possibility of capturing a wider area of the fundus.

This feature was added to the CameraApp developed, by establishing a protocol to allow the communication between Android devices and an ATmega2560 board.

Using only the CameraApp application and the micro-USB port of the smartphone, the user handling the EFS device can write specific commands, described in the applications support page, that are then converted to binary data that is sent to the serial port pf the ATmega2560 board.

This board is programmed to receive the binary data and execute specific tasks related to the light ON/OFF of the matrix LEDs, as well as the IR and white LEDs. This can be done simultaneously to the control of the UVC-Compliant Camera, that can also be plugged in the micro-USB port of the smartphone, using a USB-hub.

For acquiring images of the fundus, with the current EFS prototype, and without a NoIR camera, the white LED mentioned above is required for the illumination of the dark fundus. For patient comfort, this LED will be turned ON only during the image capture, and it needs to be perfectly synchronized with the fixation and the IR LEDs, so that these do not interfere with the acquisition, causing unwanted aberrations. For this to be possible, and for the patient to keep its eye focused on the target, the acquisition must be done under 15ms, the time response for the human eye.

Given this period of time is so small, two modes were set, given the necessity of fixating the EFS prototype in front of the patients eye prior to the acquisition.

This way, the communication protocol included in CameraApp, for the control of Internal Fixation Targets includes a Testing mode, for the user to center the retina before capturing, and an Acquisition mode, that automatically photographs the fundus.

As for the low-level control of the camera, a settings menu is also available in the application developed, with the possibility to enable/disable auto-focus, adjust brightness, contrast and gamma values. Besides, it is possible to select High temperatures White Balance. Despite this, for the full control of the image sensor parameters, ISO, shutter speed and aperture control must be added. This features are important, given the photographs of the human fundus are made in low-light environment conditions.

Prior to this work, Fraunhofer's EFS used Enhanced Camera API for control of the smartphone camera settings. In comparison to the settings controlled by the CameraApp developed, Enhanced Camera API is able to control a wider range of smartphone camera parameters, thus this is a disadvantage of CameraApp.

Nevertheless, CameraApp successfully established the synchronous control of UVC-Compliant cameras and internal fixation point actuators, that Enhanced Camera API did not include. Besides, some control of the camera settings is also possible, despite requiring some improvements, namely referring to ISO and shutter speed control.

This constitutes a great advantage, since single field fundus pictures are many times, not enough to provide an accurate diagnosis for DR. Internal Fixation Targets solve this issue [25].

This additional communication also set the difference between CameraApp and other Android Applications for the use of UVC-Compliant Cameras, such as the Webeecam application developed by Cypress [72], thus constituting a very strong improvement point brought out by this work.

With the work developed in this thesis, and the good results obtained in terms of FOV values and image aberrations lead to the conclusion that the integration of UVC-Compliant cameras in the EFS prototype, for DR assessment it's an asset.

Such cameras can guarantee the prototype's optical alignment is better then the smartphone cameras currently used. This can be said because smartphone cameras differ greatly according to manufacturers. The main aspects of this cameras for EFS integration, such as the AFOV value, that needs to be in accordance with the one that was set out for the optical system acquisition, and the camera placement in the smartphone, cause issues that originate ergonomic difficulties. This can lead to bad images of the fundus, that originate wrong diagnosis.

Solving this issues surpasses any issues related with the inevitable project cost increase that the integration of this cameras adds, when compared to the use of a smartphone camera.

Furthermore, the addition of the internal fixation point actuators, controlled simultaneously with the UVC-Compliant cameras, using the same CameraApp application developed in this work, constitute an important improvement for EFS in terms of competition with other devices already existent in the market, as was mentioned in Section 4.1.

6.1 Future Work

The work developed in this thesis lead to important conclusions for the development of a screening device for DR assessment, as established in the begging of this Chapter. Besides this conclusions, some improvement points were also pointed out, leading to this future work section.

The prototype integration of the UVC-Compliant camera selected, as well as the Internal Fixation Point Actuators, to provide the best outcome from a perfectly aligned optical path for DR assessment should be accessed.

Low-level control of the highly parametrized camera module should be enhanced, specially for the enabling of controllable parameters such as ISO, shutter-speed and exposure time. Besides, this type of control should be more automatized, in a way that a CameraApp user could just adjust the prototype in the desired position, and the camera settings would automatically be perfected for that particular environment. This would be a very good feature for EFS, since the patient needs to keep it's eyelids open during the examination. If the user doesn't have the need to adjust the camera parameters, then the process should be much faster and commode, possibly increasing the quality of the fundus image.

Another possibility to be explored is the integration of the camera module with Fraunhofer Enhanced Camera API, so that an external UVC-Compliant cameras can be added to the library and its use can be simplified for other developers.

A set of resolution tests should be performed, given its importance for the assessment of the fundus image quality, that is one of the factors affecting the DR diagnosis.

Internal fixation target actuators should be enhanced in the future by replacing the current electronics, constituted by the Arduino Mega ATmega2560 and LED matrix by a BackPack with integrated eletronics [1]. This would diminish any issues related with the bad connections of those two components due to ruined wires, for instance, and make the prototype more compact.

[1] https://www.adafruit.com/product/870

6.1.1 Resolution Tests

As described in Subsection 4.2.3, Resolution and Color Depth represent two factors, that have major influence in the quality of captured images. If image resolution is not good enough, it may not detect structures related to DR, such as microaneurysms, that in early stages where treatment is more effective, have sizes in the order of μm.

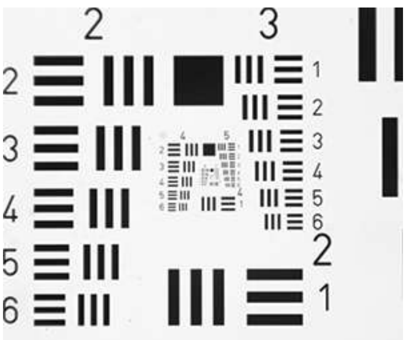
This way, as future improvements of this work, an array of tests must be performed, by the use of specific targets that can evaluate with high accuracy if the imaging system quality is enough to be used as a diagnosis method for DR assessment.

Since this targets were not available during the course of this thesis, the tests couldn't be performed, but a protocol is here suggested in order to conclude this task.

To accurately measure Resolution, targets such as 1951 USAF Resolution Targets can be used, since these constitute a standard test for imaging systems. This targets consist on three vertical and three horizontal bars, equally spaced from each other. The resolution is the measured based on the bar width and space, where the length of the bars is equal to five times the width of a bar. Vertical bars are used to calculate horizontal resolution and horizontal bars are used to calculate vertical resolution [73].

By then, resolution can be measured quantitatively, in terms of line per millimeter (lp/mm), applying Equation 6.1 to the measurements obtained. *GroupNumber* and *ElementNumber* indicate the group and element number of the bars that are starting to look blurred in the photograph taken with the imaging system's camera. An actual representation of group and element numbers is represented in Figure 6.1a [73].

$$Resolution(lp/mm) = 2 * (GroupNumber + \frac{ElementNumber - 1}{6}) \tag{6.1}$$



a 1951 USAF Resolution Targets [73].

b X-Rite ColorChecker [74].

Figure 6.1: Resolution test targets suggested for implementation as future work.

Color depth tests take in consideration the true color balance of the acquired image. This kind of tests consist on photographing a color palette, as the X-Rite ColorChecker [2], provides a non-subjective comparison with a test-pattern of 24 specifically prepared

[2]https://www.xrite.com/pt-pt/categories/calibration-profiling/colorchecker-passport-photo

colored squares, Figure 6.1b. Each color square represents a natural object color, such as the human skin, blue sky colors, amongst many others, to provide a qualitative reference to quantitative values [75].

The quantitative analysis is done by measuring the Dynamic Range of the imaging system. This can be done by comparison of the color target and the image captured with the imaging system [76].

In order to assure the best results, the tests mentioned should be applied after the integration of the UVC-Compliant camera and the Internal Fixation Target Actuators in the prototype, as the optical alignment presents major impact on image quality, thus it should be specific for the camera integrated.

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